ARCHIVES OF OPHTHALMOLOGY

VOLUME 25 (old series Volume 82) MAY 1941 NUMBER 5

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RESULTS OF SURGICAL TREATMENT OF PARALYSIS OF THE SUPERIOR OBLIQUE AND SUPERIOR RECTUS MUSCLES

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If one may judge by the number of patients with paralysis of the superior oblique and superior rectus muscles who present themselves after consulting reputable ophthalmologists without any prospect of relief, it would seem that the surgical treatment of paralytic squint is not yet on a sound and widely recognized basis. This is a pity, since there are few conditions in which an accurate diagnosis and the use of simple and definitely indicated surgical procedures are rewarded with more pleasing results.

It was with this thought in mind that the following report of cases was prepared. It includes all the cases in my practice during the last eight years in which a definite diagnosis of these conditions could be made and in which operation was performed. The cases are presented in tabular form, with a discussion of certain practical points suggested by the observations. As will be seen, the series includes 2 cases in which the choice of operation may seem difficult to explain. It is frankly admitted that these operations were the result of faulty diagnosis, the proper diagnosis being made only later but, in the light of further experience, quite definitely.

The inclusion of these early cases will aid in emphasizing the primary importance of exact diagnosis in treating paralytic squint. It would seem to be a lack of perfect confidence in their methods of diagnosis which makes many ophthalmologists hesitate to offer surgical relief, for it is particularly true of this condition that the proof of the diagnosis is in the operative result. When the diagnosis is correct, the indicated operative procedure will be followed by at least some improvement in practically every case. When the diagnosis is wrong, everything is wrong.

In memory of Alfred Bielschowsky.

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In my own experience the chief source of error in diagnosis is dependence on textbook statements and diagrams concerning the fields of diplopia in the presence of paralytic squint. These depend on theoretic considerations and result in pictures which would be seen only in cases of very early paralysis uncomplicated by preexisting phorias and by secondary contracture of opposing muscles. Such early and uncomplicated paralyses are, as a matter of fact, rarely seen. How many diagnoses have been missed because of belief in the statement that paralysis of the superior oblique muscle is followed by homonymous diplopia since the muscle is an abductor! This statement neglects the essential fact that the abducting function of this muscle is of minor importance and may be entirely neutralized by a preexisting exophoria, so that the diplopia associated with paralysis of the trochlear nerve is not uncommonly crossed or may be crossed in the right field and uncrossed in the left. How many cases of paralysis of the trochlear nerve have been missed by belief in the statement that diplopia is always more marked in the lower inner field of the paralyzed eye or, as might be gathered from the diagrams, only in this field! It is true that this is the field of maximal action of the superior oblique muscle, but it is also true that in nearly every case of paralysis of this muscle the inferior oblique undergoes secondary contracture, which results in marked diplopia in the upper inner field or in the whole field of motility. Indeed, the most striking feature in many cases is the marked upshoot of the paralyzed eye in adduction, which becomes most marked on looking up and in. This sign may even persist when the original paralysis has almost completely recovered, so that it is almost the only sign which indicates the original paralysis.

The method of examination described by the late Alfred Bielschowsky is in my opinion the only one which avoids the pitfalls of stereotyped textbook diagrams. As he first described it in 1907,[1] illustrated as this description was by exact details of the observations in numerous actual cases and accompanied as it was with consideration of the common complicating factors, the method is so simple as to convert a realm of speculation into a field of practical diagnosis. As described in his lectures, published in American journals during the last few years and recently collected in a monograph,[2] the method is not quite so easy

1. Bielschowsky, A.: Die Motilitätstörungen der Augen nach dem Stand der neuesten Forschungen, in Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1907; in Axenfeld, T., and Elschnig, A.: Handbuch der gesamten Augenheilkunde, Berlin, Julius Springer, 1939, vol. 8, pt. 1, chap. 11, supp. 1, pp. 5-557.

2. Bielschowsky, A.: Lectures on Motor Anomalies of the Eyes: I. Physiologic Introduction, Arch. Ophth. **12**:805-818 (Dec.) 1934; II. Paralysis of the Individual Eye Muscles, ibid. **13**:33-59 (Jan.) 1935; III. Paralyses of the Conju-

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to understand, but its essential features are available. I have attempted to give a concise summary of this method, with the clinical findings associated with the various paralyses, in my textbook.[3] It consists in a careful objective study of the ocular deviations in the various fields, with study of the subjective diplopia and tipping of images as the next step, for confirmatory or corrective evidence. In most cases study of the deviations alone will permit a diagnosis of the paralyzed muscle, which will be confirmed by a study of the diplopia.

With slight paresis the deviation may be so small that the diagnosis is not certain without a study of the diplopia. In this study the use of a long horizontal line instead of the usual vertical one is an essential detail. This adds one more mental adjustment on the part of the examiner, since he must mentally rotate the horizontal image through 90 degrees to visualize the upper pole of the eye. It is well worth this additional effort, however, since vertical images often overlap in such a way that the distinction of the two images is extremely difficult, while fusion of the images occur so that tipping is difficult for some patients to observe. There are so many pitfalls in the study of diplopia, resulting from the patient's poor cooperation or from misunderstanding between the patient and the physician, as to make its use in many cases barren of results. To cover one eye with a red glass as the first step in diagnosis is to cover up valuable evidence by making actual deviation or limitation of motion invisible.

Bielschowsky's method [3a] is no short cut to knowledge but demands careful observation and a certain power of deduction on the part of the physician. It depends not on the memorizing of rules but on a thorough familiarity with the action of the muscles in the various fields of rotation.

A few general principles which are especially useful may be recalled:

1. When a difference between the deviation of the two eyes on cover test can be determined, the eye showing the smaller deviation is the paralyzed eye.

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gate Movements of the Eyes, ibid. **13**:569-583 (April) 1935; IV. Functional Neuroses: Etiology, Prognosis and Treatment of Ocular Paralysis, ibid. **13**:751-770 (May) 1935; Disturbances of the Vertical Motor Muscles of the Eyes, ibid. **20**:175-200 (Aug.) 1938; Lectures on Motor Anomalies: I. The Physiology of Ocular Movements, Am. J. Ophth. **21**:843-854, 1938; II. The Theory of Heterophoria, ibid. **21**:1129-1136, 1938; III. The Signs and Symptoms of Heterophorias, ibid. **21**:1219-1229, 1938; IV. The Etiology of Strabismus, ibid. **21**:1329-1342, 1938; V. Development and Causes of Strabismus, ibid. **22**:38-43, 1939; VI. Principles of Surgical Treatment, ibid. **22**:145-153, 1939; VII. Paralyses: General Symptomatology, ibid. **22**:279-288, 1939; VIII. Paralysis of Individual Eye Muscles; Abducens Nerve Paralysis, ibid. **22**:357-367, 1939; IX. Oculomotor Nerve Paralysis and Ophthalmoplegias, ibid. **22**:484-498, 1939; X. Supranuclear Paralyses, ibid. **22**:603-613, 1939; Lectures on Motor Anomalies, Hanover, N. H., Dartmouth College Publications, 1940.

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2. When the vertical deviation of the paralyzed eye is greatest in adduction, an oblique muscle is involved. When it is greatest in abduction, one of the vertical rectus muscles is involved.

3. The image of the paralyzed eye is always seen in the direction in which the affected muscle should move the eye. This applies to tipping of images, and hence it is easy to remember that with paralysis of the right superior oblique muscle the upper pole of the right image is tilted to the left.

4. When tilting of images is marked and when tipping the head greatly increases diplopia, an oblique muscle is nearly always involved.

5. The principal action of a muscle should be primarily considered in the diagnosis of paralytic squint. Subsidiary actions, especially the horizontal action of the oblique and the vertical rectus muscles, must not be considered of importance, as they may be neutralized by preexisting phorias.

The present discussion is limited to paralysis of the superior oblique and superior rectus muscles because, aside from paralysis of the abducens nerve, which has been discussed in another paper,[4] these are the forms of isolated muscle paralysis most commonly observed. During the period covered by these cases I have observed only 1 case of isolated paralysis of the inferior rectus muscle and 2 of paralysis of the inferior oblique muscle. None of the patients have come to operation. The tables list 8 cases of paralysis of the trochlear nerve and 5 of paralysis of the superior rectus muscle in which operation was performed. In addition to these cases, 7 cases of paralysis of the trochlear nerve and 8 of paralysis of the superior rectus muscle were observed in which operation was not performed by me. In most cases the paralysis was either temporary (when due to a vascular lesion) or so slight as to be satisfactorily corrected by prisms. Two cases were observed in consultation; the patients were operated on by other ophthalmologists. One of these cases is deserving of a note, as it illustrates the persistence with which error, once arrived at, may be upheld. The patient was a girl aged 9 years whose mother had kept a careful record of previous findings and operations. The child had shown left hypertropia since infancy. To correct this, a cinch of the left inferior rectus muscle had been done at the age of 5 years, with no improvement. Later a cinch of the right superior rectus muscle had been done, and finally a recession of the left superior rectus muscle had been performed. The effect of all these operations, according to the records, had been nil. When I saw the child, the typical

3. Gifford, S. R.: A Textbook of Ophthalmology, ed. 2, Philadelphia, W. B. Saunders Company, 1941.

3a. The method is essentially the same as that described by Duane and later by White.

(Footnotes continued on next page)

picture of partial paralysis of the left superior oblique muscle with overaction of the left inferior oblique muscle was present. Myotomy of the left inferior oblique muscle was advised and was performed by Dr. Andrew Browning, of Portland, Ore. It resulted in reducing the left hypertropia from 10 prism diopters to right hyperphoria of 4 prism diopters. The tilting of the head had almost entirely disappeared, and the child was comfortable. Diplopia was present only in the upper right quadrant. Similar instances of mistaken diagnosis are seen in cases 1 and 2 (table 1). In both cases hypertropia was present, and for want of familiarity with Bielschowsky's method what can now be reconstructed as partial paralysis of the superior oblique muscle with overaction of the inferior oblique muscle was missed. A tentative diagnosis of spasm of the superior rectus muscle was made in both cases, a condition which must now be recognized as exceedingly rare, if indeed it ever occurs alone. Thanks to an excellent fusion faculty in both cases, the poorly chosen operation, recession of the superior rectus muscle, resulted in considerable improvement. In the second case a second poorly chosen operation, tucking of the inferior rectus muscle, resulted in a perfectly satisfactory field of binocular vision. In both cases myotomy of the overacting inferior oblique muscle would probably have given a better functional result. Recession of the superior rectus muscle is certainly not indicated as the primary operation for paralysis of the superior oblique muscle, and the fact that the results were no worse in these cases must be ascribed to an intercession of Providence in behalf of the well meaning but erring ophthalmologist. It must be considered possible that overaction of the superior rectus muscle may occur together with that of the inferior oblique muscle after paralysis of the superior oblique muscle and that this may be a factor in causing diplopia all over the field. It is certainly logical, however, to perform myotomy of the inferior oblique muscle first when this muscle is definitely overactive. If the effect is insufficient, recession of the opposite inferior rectus muscle is the operation which should usually be chosen, as this muscle is the true synergist of the superior oblique. Only if this fails and the paralyzed eye remains in sursumvergence in the primary position should recession of the superior rectus muscle be considered. In a case of complete paralysis of the trochlear nerve with marked hypertropia, such as occurred in case 3, it may have been necessary to perform recession of the superior rectus muscle. This was done, with advancement of the inferior rectus muscle, which improved the deviation only from 35 prism diopters to 27 prism diopters. It was necessary later, however, to perform myotomy of the inferior oblique muscle, which

4. Gifford, S. R.: Muscle Transplantation for Paralytic Strabismus, Arch. Ophth. **2**:651-657 (Dec.) 1929; Tendon Transplantation for Paralysis of External Rectus Muscle: Further Report, ibid. **24**:916-923 (Nov.) 1940.

TABLE 1.—*Paralysis of the Superior Oblique Muscle: Operative Cases*

Case; Patient; Date of First Operation	Age	Cause	Maddox Test Before Operation	Diplopia Before Operation	Operation	Maddox Test After Operation	Diplopia After Operation	Additional Notes
1 Nell B. 1933	26	Congenital	R. hyperphoria 8 D.; exophoria 3 D.	Diplopia in left	Recession of R. superior rectus	R. hyperphoria 2 D.; exophoria 1 D.	Only in extreme upper left	Fair result in spite of poor choice of operative procedure; slight paresis
2 John P. 1934	42	Congenital	L. hyperphoria 15-20 D.	Diplopia in lower field and upper right	Recession of L. superior rectus; tuck of L. inferior rectus	L. hyperphoria 5 D.	Only in extreme upper right	Fusion training before and after operation seemed to help in obtaining a good result in spite of poor choice of operative procedures
3 Geo. B. 1935	18	Congenital	R. hyperphoria 30-35 D.	Diplopia all over field except with marked head tilting	Recession of R. superior rectus; advancement of R. inferior rectus; tenotomy of R. inferior oblique	R. hyperphoria 15 D.	Fuses with head straight; diplopia in looking left	No result from first 2 operations; fair result from tenotomy of R. inferior oblique; should have recession of L. inferior rectus
4 E. K. 1936	15	Congenital	R. hyperphoria 22 D.	Diplopia all over field	Tenotomy of R. inferior oblique	R. hyperphoria 20 D.	Diplopia only in lower part of field	
5 Mrs. S. 1937	39	Congenital	L. hyperphoria 30 D.	Tilts head to avoid diplopia	Tenotomy of L. inferior oblique	L. hyperphoria 20 D.	Diplopia only in in upper right	Holds head straight upshoot of left eye; fusion relieved in primary position
6 Billy S. 1938	11	Congenital	R. hyperphoria 20 D.	All over field except when tilting head	Tenotomy of R. inferior oblique	R. hyperphoria 6 D.	Diplopia in lower left	Upshoot in adduction and head tilting relieved
7 Arthur B. 1938	9	Congenital	Not measured	Tilts head to prevent diplopia	Tenotomy of L. inferior oblique; later, recession of R. inferior rectus and second tenotomy of L. inferior oblique	L. hyperphoria 8 D.; exophoria 6 D.	No diplopia with 3 D. base down right and up left	Upshoot in adduction relieved after second operation; also head tilting
8 Richard M. 1938	4	Congenital	L. hyperphoria 15-20 D.	Tilts head to avoid diplopia	Tenotomy of L. inferior oblique	Exophoria 2 D.; L. hyperphoria 3.5 D.	Eyes level in primary position	Slight supshoot in upper right

further reduced the deviation to a hyperphoria of 15 prism diopters. The patient can fuse and holds the head straight but suppresses at times, when the right eye turns up. Recession of the opposite inferior rectus muscle would further improve the condition.

It will be noted that in most of the cases of paralysis of the trochlear nerve overaction of the inferior oblique muscle was a marked feature and that myotomy of this muscle alone produced so much relief that recession of the opposite inferior rectus muscle was seldom required. The power of fusion in such cases is sometimes surprising. Case 5, for example, was that of a woman of 35 who had been examined by reputable ophthalmologists at intervals since childhood. Glasses had been prescribed, but no operative intervention had ever been suggested. With paralysis of the right trochlear nerve, her right hyperphoria was 36 prism diopters, and still, by moderate tipping of the head to the left shoulder, she maintained fusion with a fair degree of comfort. When she looked to the left or straightened the head the right eye showed a marked upshoot and diplopia was pronounced. The habitual tilting of the head was disfiguring and uncomfortable. After myotomy of the right inferior oblique muscle the right hyperphoria in the primary position was reduced only to 20 prism diopters, but fusion was maintained with the head straight, and diplopia occurred only on looking to the extreme left. Further relief by recession of the opposite inferior rectus muscle was declined, as the patient was satisfied. In case 7, however, temporary relief after myotomy of the left inferior oblique muscle was followed by recurrence of the head tilting and the upshoot in adduction after two months. Recession of the right inferior rectus muscle (5 mm.) was accompanied with a second myotomy of the left inferior oblique muscle. The muscle was found reattached to its original insertion. It was freed carefully from its fascia, and 4 mm. was resected. The result, after eight months, is left hyperphoria of 8 prism diopters, with good fusion in the primary position and relief of head tilting. In case 6, right hypertropia of 20 prism diopters was reduced to right hyperphoria of 6 prism diopters by myotomy of the right inferior oblique muscle alone, and a good field of binocular vision is present without prisms. In case 8, left hypertropia of 20 prism diopters was reduced to left hyperphoria of 3.5 prism diopters by myotomy of the left inferior oblique muscle. Diplopia was present only in the upper right field. It is difficult to explain why the effect of myotomy of the inferior oblique muscle has varied so greatly in different cases. Apparently reattachment of the muscle to its insertion depends on certain fortuitous circumstances which are beyond the control of the operator. The technic followed in these cases has included exposure of the origin, freeing of all fascial attachments and resection of 4 to 5 mm. close to the origin, according to Bielschowsky's advice. Judging from a limited experience in cases of

concomitant squint with tenotomy of the muscle at its attachment to the globe, a greater effect can be expected from treatment by this means, and this method should probably be preferred in cases of marked overaction.

I have not been courageous enough to attempt recession of the inferior oblique muscle as described by Wheeler or advancement and resection of the superior oblique muscle, which he also described.[5] On account of the extensive insertions of these muscles in areas far back on the globe, these operations must impress many ophthalmologists as exceedingly difficult of execution. While in all the operative cases paralysis of the trochlear nerve was congenital, isolated paralysis of the superior rectus muscle was less commonly so. In only 1 case (case 5) was it congenital; in 1 it was due to fracture of the skull, in 1 to direct orbital trauma, in 1 to poliomyelitis and in 1 to hyperthyroidism. In the last-mentioned case (case 2, table 2) paralysis of the left superior rectus muscle was complete, while paralysis of other muscles, which had previously been present, had cleared up completely. There was left hypotropia of 32 prism diopters, and diplopia was present in all parts of the field. Myotomy of the right inferior oblique muscle produced some improvement, and resection and advancement of the paretic left superior rectus muscle caused a further reduction in the deviation to left hypotropia of 23 prism diopters. Since no limitation of motility of the right eye was produced by myotomy of the inferior oblique muscle, the muscle was exposed a second time. Some cicatricial tissue was dissected from the region of its origin, but the muscle itself could not be found. No improvement in the condition followed this procedure. The patient wears prisms of 10 prism diopters base up and down for distance, for reading no prisms are required. The appearance of the left eye, which exposed a large area of sclera beneath the upper lid, has been greatly improved by the advancement. The condition could probably be further improved by recession of the left inferior rectus muscle, but there is some doubt of this, as the superior rectus muscle is completely paretic. Transplantation of the upper halves of the internal and external rectus muscles to the insertion of the superior rectus muscle would probably give the best result but is not considered favorably by the patient, an elderly woman, who feels that she is getting along fairly well. Such paralysis following severe hyperthyroidism with malignant exophthalmos is rarely treated by operation, since not only both superior rectus muscles but usually other muscles are commonly involved. Two other cases are now under observation, however, in which only one superior rectus muscle is involved and in which operation is indicated.

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5. Wheeler, J. M.: Advancement of the Superior Oblique and Inferior Oblique Ocular Muscles, Tr. Am. Ophth. Soc. **32**:237-244, 1934; Am. J. Ophth. **18**:1-5, 1935.

TABLE 2.—*Paralysis of the Superior Rectus Muscle: Operative Cases*

Case; Patient; Date of First Operation	Age	Cause	Maddox Test Before Operation	Diplopia Before Operation	Operation	Maddox Test After Operation	Diplopia After Operation	Additional Notes
1 Mary D. 1935	31	Fracture of skull	R. hypophoria 15-17 D.; exophoria 10 D.	All over field; worse up and to right	Myotomy of L. inferior oblique	R. hypophoria 5 D.	Only in extreme upper right	No discomfort since operation
2 Mrs. W. 1937	65	Exophthalmic goiter	L. hypophoria 32 D.	Over most of field	Myotomy of R. inferior oblique; advancement of L. superior rectus	L. hypophoria 23 D.	Fairly comfortable with prisms	Complete paralysis of L. superior rectus; result only fair, but patient feels much improved
3 Miss M. 1937	21	Poliomyelitis	L. hypophoria 14 D.	Over most of field except below	Advancement and resection of L. superior rectus	L. hyperphoria 3 D.	Only in extreme upper part of field	Marked overeffect at first; still slight overeffect but comfortable
4 Mr. M. 1938	40	Trauma to left orbit	Not measured	No motion above midline; diplopia above this	Recession of L. inferior rectus; advancement and 4 mm. resection of L. superior rectus; later, replacement of inferior rectus	L. hyperphoria 6 D.	Fusion in field 40 D. above and 20 D. below midline	Marked overeffect requiring replacement of inferior rectus; still slight overeffect
5 Mr. D. 1939	27	Congenital	R. hypophoria 12 D.	Over most of field	Myotomy of L. inferior oblique	R. hypophoria 6 D.	Fairly-comfortable with 3 D. bases down right and up left	To have cinch of R. superior rectus

The most gratifying case listed in table 2 was case 1. The patient, a nurse, had been observed for three years. On account of the great variation in her statements in the diplopia tests and the nervous state which such examinations induced, a satisfactory diagnosis was not made. Prisms were prescribed which corrected the diplopia in the primary position. Diplopia was noted, however, not only above but down and to the right at all times. Professor Bielschowsky himself, in a necessarily hurried examination before a class, was unable to make a definite diagnosis but suspected paralysis of the left trochlear nerve with an overacting left inferior oblique muscle. At a later examination slight limitation of motility of the right eye on looking up and right was discovered, and right hypotropia was found to be greatest in this field. Once the tentative diagnosis of paralysis of the right superior rectus muscle was entertained, it was found that all other details fitted into the picture perfectly. Tipping of the right image was slight but was with the upper pole to the left, and diplopia was greatest in the upper right quadrant of the field. Right hypotropia measured 17 prism diopters. Immediately after myotomy of the left inferior oblique muscle all diplopia disappeared except in the extreme right upper quadrant. The patient discarded her glasses and has been comfortable ever since, in spite of a remaining right hypophoria of 5 prism diopters. In case 5 the condition was almost identical, but the result was not so satisfactory. Left hypotropia of 12 prism diopters was improved to 6 prism diopters by myotomy of the right inferior oblique muscle. The patient fuses with 3 prism diopters bases up and down but is not so comfortable as immediately after operation, and a cinch of the left superior rectus muscle, which is only partially paretic, has been advised.

Case 4 illustrates the danger of operation on the superior and inferior rectus muscle at one sitting. The patient had suffered a penetrating wound of the orbit resulting in complete paralysis of the left superior rectus muscle. There was no motion in any part of the field above the midline, and hence it was felt that the inferior oblique muscle also must be involved. The condition did not change during a year's observation; so advancement and 4 mm. of resection were performed on the left superior rectus muscle, combined with a 5 mm. recession of the left inferior rectus muscle. The result was a marked overeffect, with left hypertropia of 17 prism diopters and diplopia in the whole lower part of the field. After nine months the deviation had decreased only to 12 prism diopters; so the left inferior rectus muscle was exposed. It was found to be much contracted, almost inelastic and inserted in a line 12 mm. from the limbus. It was replaced in a scleral groove made 5 mm. from the limbus. The result nine months later was left hyperphoria of 6 prism diopters with a binocular field extending 40 degrees above and 20 degrees below the midline.

In case 3, in which the paralysis was not complete, a similar overeffect was produced by advancement and 4 mm. resection of the left superior rectus muscle alone. Right hypertropia was alarmingly great during the first few months but gradually decreased until, after one year, only right hyperphoria of 3 prism diopters was present. At the time of writing exophoria of 15 prism diopters is also present, which could be improved by a cinch of the internal rectus muscle, but the patient fuses most of the time and is satisfied.

In considering the operative indications for paralysis of the superior rectus muscle, it may seem surprising that recession of the inferior rectus muscle is so seldom advised. It would seem that overaction of this muscle would occur as frequently as does overaction of the inferior oblique muscle in cases of paralysis of the trochlear nerve and that recession of the muscle would give results comparable to those obtained by myotomy of the inferior oblique muscle in that condition. As a matter of fact, however, one seldom sees a marked downshoot of the paralyzed eye in abduction which would indicate overaction of the inferior rectus muscle. One also hesitates to perform recession on the inferior rectus muscle for fear of inducing diplopia in the important lower field, whereas the inconvenience produced by myotomy of the inferior oblique muscle, occasional diplopia in the extreme upper inner field, is inconsiderable. In the presence of partial paralysis of the superior rectus muscle, as illustrated by cases 1 and 5, myotomy of the opposite inferior oblique muscle has given results so good that it must be considered the operation of choice. The operation is performed with not more than one day's hospitalization and if an untied subcuticular suture of 0.004 Deknatel silk is used the scar is usually invisible. Suturing of the fascia with catgut has been abandoned after the formation of granulomas about the knots in several cases and has proved entirely unnecessary. In cases of more extreme paralysis, resection and advancement of the paretic muscle have given a sufficient result except in case 2. It may be reenforced by myotomy of the opposite inferior oblique muscle as a second operation or may be employed when this procedure has been performed first with insufficient effect. In cases of complete paralysis with marked hypotropia in the primary position, tendon transplantation from the two lateral rectus muscles may offer the best prospect of a good functional result and will be considered in future suitable cases. A good result was reported by Posey [6] from the use of a similar transplant in the absence of the inferior rectus muscle.

6. Posey, W. C.: The Muscle Advancement Operation, Tr. Am. Acad. Ophth. **26**:83-89, 1921.

CONCLUSIONS

1. Exact diagnosis is the sine qua non of surgical treatment of paralysis of the vertical and oblique muscles. The Bielschowsky method has given, on the whole, satisfactory results, as proved by improvement following operation.

2. Operative treatment of these conditions has proved gratifying. Patients are exceedingly grateful for any relief from diplopia and for any improvement in the binocular field, even when the result may seem to the surgeon functionally imperfect. No patient in this series regrets having undergone operation. One (case 4, table 2) was in considerable doubt for nine months but is now perfectly satisfied.

3. In cases of paralysis of the trochlear nerve, accompanied as it usually is by overaction of the inferior oblique muscle, myotomy of the homolateral inferior oblique muscle will usually be advised first and will frequently give a sufficient effect. If the effect is insufficient, recession of the opposite inferior rectus muscle will be employed. Only in cases of extreme hypertropia and after the two previously mentioned procedures should recession of the homolateral superior rectus muscle be considered.

4. In cases of moderate paralysis of the superior rectus muscle, myotomy of the contralateral inferior oblique muscle is the operation of choice and will give sufficient effect in most instances. If its effect is insufficient or if the paralysis is severe, advancement and resection of the paralyzed muscle are indicated; only if hypotropia remains marked after these procedures should recession of the homolateral inferior rectus muscle be advised.

FUNDUS OCULI IN DIABETES MELLITUS

A CLINICAL ANALYSIS OF THE APPEARANCE OF THE FUNDUS IN 2,360 CASES

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For some years in the department of metabolism at the Montreal General Hospital examination of the fundus of the eye has formed a part of the routine in all cases of diabetes. The examination has consisted in a diligent search for pathologic conditions of the interior of the eye, with special reference to the appearance of the retinal vessels. In all cases the examinations have been conducted with the pupils dilated. For uniformity of interpretation of the conditions seen, practically all the examinations have been made by myself. In this paper I cannot present much more than a brief report of the conditions found.

In a series of 2,360 cases, the following lesions were reported:

Cataract	173
Retinal hemorrhages	105
Arteriosclerosis of the retinal vessels	205
Retinitis	54
Diabetic retinitis	41
Neuroretinitis	11
Retinitis of arteriosclerosis	26
Diabetic retinitis with arteriosclerosis	28
Hypertensive retinitis	3
Macular senile changes	9
Disseminated choroiditis	3
Choroidal changes	7
Iritis	11
Glaucoma, noninflammatory	15
Atrophy of optic nerve	1
Zonular cataract	2
Interstitial keratitis	2
Folds in Descemet's membrane	1
Pannus	1
Detachment of the retina	2
Homonymous hemianopia	2
High myopia	4

From the Department of Ophthalmology, the Montreal General Hospital.

Read before the Pan-American Congress of Ophthalmology, Cleveland, Oct. 11, 1940.

Disturbances of accommodation	13
Proliferating retinitis	2
Lipaemia retinalis	1
Retinochoroiditis	2
Retinitis pigmentosa	1
Retinitis circinata	1
Large vitreous hemorrhage	1

According to the foregoing list, it will be observed that there were 476 persons among these 2,360 with retinal lesions which were more or less related to their diabetes, thus:

Arteriosclerosis of the retinal vessels	205
Retinal hemorrhages	105
Retinitis	54
Diabetic retinitis	41
Diabetic retinitis with arteriosclerosis	28
Retinitis of arteriosclerosis	26
Neuroretinitis	11
Hypertensive retinitis	3
Proliferating retinitis	2
Lipaemia retinalis	1

Diabetes is largely a disease of middle life. It therefore occurs at the age when arteriosclerosis generally manifests itself. Histologically, two types of sclerosis are found in the retinal arteries. In the larger vessels the atheromatous type of change, involving the endothelium, is the rule. It may lead to occlusion of the affected vessels. In the smaller retinal branches, which contain no elastic lamina, the more common type of sclerosis is the hyaline thickening of the media without complete obliteration of the lumen.

In this series, arteriosclerosis was graded as (1) beginning, (2) moderate and (3) severe. It was graded as beginning when there were congestion and other changes in the veins, an increased light reflex and some loss of transparency of the vessel walls; as moderate when there were more loss of transparency, moderate arteriovenous compression and irregularity in the caliber of the vessels, and as severe when the irregularity in the vessel caliber was marked, the "nicking" of the vessels easily observed and the arterial walls opaque. One has but to look carefully at the diabetic fundus to note the early changes in the retinal veins. In collaboration with Rabinowitch and Ritchie in 1934,[1] I noted: "Alterations in the vessels of the diabetic fundi affect both veins and arteries. The first sign observed is a general congestion of the veins, which results

1. Rabinowitch, I. M.; Ritchie, W. L., and McKee, S. H.: Statistical Evaluation of Different Methods for the Detection of Arteriosclerosis in Diabetes Mellitus, Ann. Int. Med. **7**:1478, 1934.

in an increase of their diameter and a broadening of their light reflex. Next, these veins being made longer by congestion, show bending in the direction of the artery, and this bending may be considered a first step in the development of venous tortuosity. This predisposes to haemorrhage." There were 204 patients whose retinal vessels showed signs of arteriosclerosis, graded as described.

Rabinowitch asked: "Is the incidence of arteriosclerosis increasing, and, if so, is the menace more apparent than real?" An apparent increase is to be expected, since other important causes of death have been greatly reduced. A little over a decade ago coma was the chief cause of death among diabetic persons. This condition is rapidly disappearing. Whether it is apparent or real, the incidence of arteriosclerosis is very high. Also disturbing is the fact that in the majority of diabetic persons with cardiovascular-renal disease the diabetes was mild. This emphasizes a well recognized fact, namely, that cardiovascular or cardiovascular-renal disease is related not to the severity but to the duration of the diabetes.

Since the time of Jaeger there has been no dispute about the frequency of retinal hemorrhages and associated waxy exudates in the retinas of diabetic persons past middle age. In our series there were 105 persons who showed only retinal hemorrhages. Some showed only two or three small hemorrhages, while others showed many more. The great majority of these patients were beyond the fifth decade. Waite and Beetham [2] found that the average age for all diabetic patients with deep retinal hemorrhages was 58 years, and in their series also considerably more than half of the hemorrhages occurred in patients with blood pressures falling within the normal range.

Diabetes is often more severe during the first three decades of life. The values for blood sugar may be considerably higher, and the insulin requirements are usually somewhat greater, than at any other time in life. Of 96 consecutive patients among the last 1,000 examined, ranging in age from 6 years to and including 31 years, the fundus was normal in all but 4. One of these had two small retinal hemorrhages; in the second there were numerous hemorrhages throughout the retina, and in the third, a woman aged 23 years, each fundus showed numerous small hemorrhages scattered over the whole retina, with here and there characteristic chalk white patches. The fourth patient, a woman aged 31 years, showed definite hypertensive retinitis with papilledema. In the other 92 cases there was no retinal pathologic change whatsoever.

As diabetes grows milder with each increasing decade, the hemorrhages become more numerous. "There is with increasing duration of

2. Waite, J. H., and Beetham, W. P.: The Visual Mechanism in Diabetes Mellitus, New England J. Med. **212**:367, 1935.

diabetes, an increasing incidence of deep retinal haemorrhages out of proportion to the accompanying increase in the age of the patient, as reflected in the average age group." Insulin has repeatedly been named as a potential cause for retinal hemorrhage in diabetic persons. Waite and Beetham [2] stated that their experience would indicate that the only danger from insulin in this connection lies in withholding it.

While there is a marked similarity between diabetic retinitis, retinitis due to renal disease and arteriosclerotic retinitis, there are not many cases in which it is possible to state dogmatically from an ophthalmoscopic examination alone that retinitis is due to diabetes. Nevertheless, Moore [3] expressed the belief that there are features which, while they are not pathognomonic when combined, form a picture which is sufficiently characteristic to enable one to attribute the condition to diabetes. With this view I agree. These features are: 1. The patches of retinal exudate in cases of diabetes tend to have sharp-cut edges, are often solid and soapy or waxy looking, are usually distributed in an irregular manner and sometimes form an irregular ring wide of the macule. 2. A star figure is uncommon and, if present, does not acquire the degree of symmetry that may be seen in cases of retinitis due to renal disease. 3. The soft-edged cotton wool patches, so frequent in cases of severe renal retinitis, do not appear in cases of diabetic retinitis. Retinal edema is never so marked; so retinal detachment does not result. 4. Retinal hemorrhages are generally in the deeper retinal layers and therefore are roughly circular in outline instead of being flame shaped. 5. Circular retinal pigment spots, which are not rare in the later stages of retinitis due to renal disease, are not seen, I think, in cases of diabetes.

In the series of persons whose examinations are reported here, there were 41 who were thought to have diabetic retinitis. An additional 28 were thought to have diabetic retinitis associated with a definite state of retinal arteriosclerosis. Cases 1 and 2 exemplify what I have designated as diabetic retinitis. It is to be emphasized that the diagnosis in these cases, as in all the others, was wholly ophthalmoscopic.

CASE 1.—H. L., a man aged 55 years, with diabetes mellitus, was described as follows: "The right eye showed the media clear; the disk was flat and of good color and the margin clear; the vessels were normal in appearance. Scattered throughout the fundus were numerous small round hemorrhages, often occurring in clusters. There were also many sharply defined, white, clearly outlined areas, also in clusters. The left eye showed dustlike opacities in the anterior part of the vitreous, and the retinal picture was similar to that of the right eye; it was, however, more marked. The hemorrhages extended farther to the periphery of the retina, and at the lower temporal quadrant there was one large retinal hemorrhage. Changes of any kind in the vessels were notably absent. The blood pressure was 125 systolic and 80 diastolic."

3. Moore, R. F.: Medical Ophthalmology, ed. 2, London, J. A. Churchill, 1925.

CASE 2.—Concerning H., a man aged 73 years, the following notes were made: "Numerous small, brown hemorrhages were seen scattered over the retina, with chalk white areas here and there between. The latter were especially marked in the macular region. The retinal vessels showed no pathologic change."

Comment.—There were also 28 patients with diabetic retinitis and definite cardiovascular-renal disease. Together with the ordinary picture of diabetic retinitis, there were present in these cases the distinguishing signs of retinal arteriosclerosis. Practically all of the patients had passed the sixth decade of life.

During the years of these examinations I looked expectantly on many occasions for lipaemia retinalis. I found it on one occasion only:

CASE 3.—J. D., a boy aged 14 years, with diabetes of two years' standing, was admitted to the service of Dr. C. P. Howard on June 2, 1931. On his admission, physical examination gave essentially negative results except for (*a*) acidosis, (*b*) paronychia and (*c*) marked xanthomas. The urine contained large amounts of sugar, acetone bodies, albumin and granular casts. The blood was obviously hyperlipemic, and the first analysis yielded the following values: sugar, 0.37 per cent; cholesterol, 1.04 per cent; fat, 9.24 per cent; urea nitrogen, 13 mg. per hundred cubic centimeters; van den Bergh reaction, 0.2 unit; red blood cells, 4,260,000 per cubic millimeter, and hemoglobin, 110 per cent. The Wassermann reaction was negative.

The results of the examination of the fundus on admission were as follows:

The two fundi were alike. The disks were dirty white and slightly hazy, and the small vessels were not well seen. The arteries and veins on the disk were salmon pink and indistinguishable from one another. They were engorged and increased in size to about one and one-half times the normal. The light streak was absent. While the large vessels on the disk and those near it were salmon pink, the most striking feature of the fundus was the milky white appearance of the vessels from about 1½ disk diameters from the disk to the periphery. These vessels looked exactly as if milk had been poured into them. The retina was transparent, and the choroidal circulation showed well. The macula was well made out, and the foveal reflex was present. There were no areas of exudation, no retinal hemorrhages and no signs of inflammation of any kind in the fundi. Vision in the right eye was 6/6 and in the left 6/36, with about 3 D. of hyperopia uncorrected. The fundi had not become perfectly normal when the value for blood fat had decreased to 1.13 per cent. It would appear, therefore, that the condition was not entirely due to the hyperlipemia. It has been suggested that some temporary change in the walls of the vessels may have been a contributing factor.

In reporting this case, Rabinowitch and I [4] summarized it as follows: "The level of blood fat at which the condition disappeared was below that previously recorded. Blood fat analyses and other data obtained daily and correlated with the ophthalmoscopic examinations suggest that the condition is also influenced by factors other than the degree of lipaemia. The condition which theoretically leads to lipaemia, namely, a general cachectic condition affecting all cellular functions, including permeability, is suggested as a contributing factor."

4. McKee, S. H., and Rabinowitch, I. M.: Lipaemia Retinalis, Canad. M. A. J. **25**:530, 1931.

Friedenwald [5] stated:

With regard to the retinal as well as to the other ocular lesions found clinically in association with diabetes, there arises the difficulty of distinguishing between the direct effects of diabetes through premature senility and arteriosclerosis which it produces. All sorts of senile and arteriosclerotic retinal lesions occur in diabetics as well as in non-diabetics, but none of these lesions are found in diabetes free from arteriosclerosis. Nevertheless, it seems definitely established that there is one particular form of retinitis which occurs much more frequently in these arteriosclerotics who have diabetes than in those who do not, and it would seem at least that there is some causal connection between the diabetes and the type and distribution of the arteriosclerotic process that accompanies it. This is the so-called diabetic retinitis.

Duke-Elder [6] stated:

It is reasonable to suppose that the deficient circulation in arteriosclerosis may tend to introduce differentiating peculiarities, and that in diabetes the upset in the water balance which in the lens gives rise to acute myopia, and later to diabetic cataract, and in the posterior epithelial layers of the iris produces an oedematous disturbance, should be able to influence in a similar manner the backward continuation of this layer in the retina, producing on occasion manifestations of the disease in this tissue with clinical characteristics of its own—diabetic retinitis.

There is considerable difference of opinion regarding the basic cause of diabetic retinitis. One group believes that the yellow spots combined with the various types of small hemorrhages are a distinct entity due to toxic or biochemical changes incidental to the diabetes. Others believe that arteriosclerosis is the important causative factor. The white spots, often seen, represent fatty and hyaline degeneration, not inflammation. Buffington stated that these are not peculiar to diabetes. He also stated the opinion that the uniform venous changes seen in persons with diabetic retinitis are a direct result of this particular metabolic disease and not a sequence of vascular sclerosis.

The records of large clinics for diabetes [7] indicate that with the introduction of insulin coma has largely disappeared as a cause of death. On the other hand, insulin appears to have had no favorable effect on the mortality from cardiovascular complications. As a matter of fact, the data from such clinics clearly indicate that cardiovascular disease is the chief cause of death when consideration is given to the fact that, regardless of whether the patient died of cerebral hemorrhage, gangrene, coronary thrombosis, heart failure or angina pectoris, death was due to cardiovascular disease. The only means of controlling this condition is

5. Friedenwald, J. S.: The Pathology of the Eye, New York, The Macmillan Company, 1927.

6. Duke-Elder, W. S.: Recent Advances in Ophthalmology, London, J. & A. Churchill, 1927.

7. McKee, S. H.: Observations on the Fundus Oculi in Diabetes Mellitus, Based upon a Study of 1,272 Cases, Canad. M. A. J. **29**:520, 1933.

to detect it in its early stages. For this reason a careful physical examination is essential, including estimation of the blood pressure, measurement of the size of the heart, etc. In spite of the most careful examination, however, one may fail to detect arteriosclerosis in many cases. Roentgen examination of the blood vessels of the feet for the detection of calcification is a routine in the clinic for diabetes at the Montreal General Hospital. Such examination may also fail in many cases. The routine, therefore, includes examination of the fundi. Experience has shown that such examination is not an adjunct but a necessity, since arteriosclerotic changes in the finer blood vessels may be found long before the roentgen ray shows calcification in the arteries of the feet and also before there is hypertension, enlargement of the heart or any other clinical sign of arteriosclerosis.

Dr. I. M. Rabinowitch gave me permission to observe the cases included in this study.

OCCLUSION HYPERTROPIA

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On occasions like this it is customary for the speaker to say that he is overcome by the honor conferred on him. Whenever possible I depart from such traditional practice, but tonight I cannot do so, for I sincerely feel highly honored by the privilege of paying tribute here to the memory of Dr. de Schweinitz. I appreciate this privilege especially because of my admiration for him and because of our long friendship. This friendship began forty-one years ago, at the outset of my ophthalmologic career, when Dr. de Schweinitz was at the pinnacle of success. At that time and many times later his encouragement of my efforts in research provided a lasting inspiration for which I shall always be grateful.

The subject of this paper is of some practical importance, but I have chosen it not for this reason but because after having been perplexed by it for years, I believe that I can now contribute toward the solution of its problems.

As is well known, there exist persons who present the peculiar anomaly that when the eyes are alternately covered the covered eye deviates upward. In some of these persons, when neither eye is covered there is bifixation, and hence there is no deviation of one eye with respect to the other. In others, when neither eye is covered there is ordinary strabismus, which differs in degree and in kind in different persons. In cases in which there is bifixation the term anophoria [1] has been applied to the anomaly, on the assumption that both eyes tend to turn upward during bifixation. Stevens,[2] however, who devised this term, applied it to an entirely unrelated condition concerning which his hypotheses and speculations seem too improbable to be discussed here. On the same assumption, others have called the anomaly double

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de Schweinitz Lecture, Philadelphia, Nov. 20, 1940.

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1. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1932, vol. 1, p. 613.

2. Stevens, G. T.: A Treatise on the Motor Apparatus of the Eyes, Philadelphia, F. A. Davis Company, 1906. Stevens, G. T.: On Double Vertical Strabismus and Symmetrical Vertical Deviation of Degrees Less Than Strabismus, Ann. d'ocul. **113**:385, 1895.

hyperphoria. It is now most commonly called alternating hyperphoria, although this term implies that during bifixation the eyes alternately tend to deviate upward. Obviously, all these terms are based on the assumption that this anomaly is analogous to ordinary so-called hyperphoria in which one eye when alone covered deviates vertically in one direction, and the other eye when alone covered deviates vertically in the opposite direction. Since, as I shall point out, the real anomaly is the same whether bifixation exists or not, and the upward deviation under cover is not, as in ordinary so-called hyperphoria, simply due to abolition of bifixation, this assumption is erroneous and these terms are misleading misnomers.

The anomaly as it exists in cases of strabismus was termed by Stevens [3] anatropia, by others double hypertropia and by still others alternating hypertropia. In this connection the terminology is less objectionable, although still misleading, because it conveys the erroneous impressions that the anomaly is closely analogous to ordinary strabismus and that an upward deviation always exists while neither eye is covered. There are, however, rare cases of strabismus in which the term alternating hypertropia is accurately descriptive. In these, the patient can alternately fixate with either eye at will, and the nonfixating eye often or always deviates upward, whether covered or not. A serious objection to this term even when it is restricted to such cases is that it does not imply that the essential anomaly concerned is the same as that observed in cases in which neither eye usually deviates upward unless covered.

A term which describes the anomaly in all cases in which it may exist is obviously desirable. I suggest the term occlusion hypertropia, meaning a condition in which occlusion results in the eye assuming a position higher than that attributable to vertical phoria or tropia. The condition may be unilateral, or it may be bilateral in equal or unequal degrees. Usually it is bilateral and may then be termed alternating.

In cases of strabismus in which one eye or the other deviates upward constantly or at times even when not covered, it might be thought that alternating occlusion hypertropia is an unsuitable designation. But in such cases, when one eye is deviating upward the other eye instead may be made to deviate upward by occluding it. Smilarly, in a case of unilateral occlusion hypertropia in which the affected eye, even when not covered, deviates upward constantly or at times, occlusion is necessary to demonstrate the real anomaly. For when the deviating eye comes down it may be made to go up by occluding it, and in cases in which it never comes

3. Stevens also employed the term katatropia to designate a condition in which each eye deviated downward when covered. I have never encountered such a condition and suspect that it was purely hypothetic and was employed by Stevens simply to complete his classification. He depicted patients with the upward deviation but none with the downward.

down under ordinary conditions occlusion of the other eye reveals the fact that the latter when occluded does not deviate downward as in a case of ordinary hypertropia. In other words, whether the anomaly is associated with heterotropia or with heterophoria, its demonstration requires occlusion. It is true that to demonstrate the anomaly in cases of heterophoria with or without hyperphoria other tests, to be described later, must be employed in addition to simple occlusion, but in my opinion the advantages of the term occlusion hypertropia greatly outweigh this objection. It is to be noted that one of these advantages is that of designating the anomaly by the procedure essential for its demonstration without conveying any implication as to its cause.

In a case of heterotropia, the amount of occlusion hypertropia is the amount of upward change in deviation that occurs when the nonfixating eye is covered. In a case of heterophoria, the amount of occlusion hypertropia may be determined for the tested eye by deducting the real hyperphoria from, or by adding the real hypophoria to, the amount of upward deviation (presumptive hyperphoria [4]) under cover. The accuracy of the determination therefore depends on the accuracy with which the real hyperphoria or hypophoria can be estimated. Generally, when occlusion hypertropia exists in a case of heterophoria it is of the alternating type, and the occlusion hypertropia for each eye is approximately equal to the lesser of the upward deviations under cover, while the real hyperphoria is approximately equal to the difference between the two upward deviations. If in any particular case prismatic correction of this amount of hyperphoria causes diplopia or discomfort, these assumptions are obviously incorrect for that case, and other tests, to be described, must be employed.

Since in cases of ordinary presumptive hyperphoria it is undoubtedly the bifixation mechanism that brings the deviating eye down when uncovered, the question arises whether this is to any extent true in cases of occlusion hypertropia. First I shall consider this question as it concerns the cases of occlusion hypertropia with heterotropia.

Experimental observations on normal persons show that when suitable horizontal contours are provided vertical bifixation (sursumduction) occurs even in the absence of horizontal bifixation. To this fact the unreliability of the diplopia test for presumptive hyperphoria is sometimes due. Despite the ready elicitation of sursumduction in normal persons, when it fails by about 1 prism diopter to accomplish its function it entirely ceases to act, either at once or after acting intermittently a few times. Moreover, these observations show that its range is usually

4. By the term presumptive hyperphoria I mean the deviation commonly termed hyperphoria. My reasons for the employment of this term are given in a recent paper (Verhoeff, F. H.: Hyperphoria Tests Based on a New Principle, Arch. Ophth. **22**:743 [Nov.] 1939).

very slight, rarely more than 4 prism diopters. It may be urged, however, that this range might be greatly increased in unusual cases, such as those under consideration, but it is to be noted that large amounts of sursumduction occur only in cases of persons who habitually successfully bifixate. On the contrary, in ordinary cases of strabismus in which either eye habitually deviates, even to a minimal extent, not the slightest sursumduction exists, as is demonstrated by the fact that the deviation remains the same whether the deviating eye is covered or not. The evidence afforded by the cover test is confirmed by the fact that in these cases and also in the cases of occlusion hypertropia with strabismus a prism, base up or base down, of suitable strength when placed before the nonfixating eye will not cause any ocular movement. Since occlusion hypertropia with heterotropia is a condition in which one eye habitually deviates even when neither eye is covered, it is safe to conclude that in these cases bifixation is not concerned.

Next I shall consider the question as it concerns the cases of occlusion hypertropia with so-called orthophoria or heterophoria. These are the cases in which the term alternating hyperphoria is commonly used on the assumption that the deviations under cover are entirely due to the release of bifixation. That this assumption is erroneous I have demonstrated in a few typical cases by the following simple procedures: First, determine by the use of prisms and the cover test the deviation of one eye under cover. Then, neither eye being covered, before this eye place a rotary prism and rotate it so as to produce the effect of a base-up prism of gradually increasing power. When the prism has reached a certain power, the eye after having deviated downward in accordance with the prism will deviate upward, and in some cases the patient will observe vertical diplopia. The condition has been converted into occlusion hypertropia with vertical strabismus. Now cover the eye. Usually the eye deviates considerably farther upward, thus clearly indicating that at least this additional upward deviation was not due to release of bifixation. Sometimes this demonstration fails, because the prism itself brings into action the monocular conjugate mechanism. A negative result is therefore of no importance. Of course, if the case is not really one of occlusion hypertropia the demonstration will always fail. Usually it succeeds at the first attempt and fails in some of the subsequent attempts made shortly afterward.

I have found that a prism base in or base out is unsatisfactory for the test because, owing to the greater prism power required to produce horizontal diplopia, the prism is apt to abolish the action of the binocular conjugate mechanism together with that of the bifixation mechanism. After the condition has been converted into occlusion hypertropia with strabismus, the problem becomes the same as that just previously considered. In cases of occlusion hypertropia, as in cases of ordinary pre-

sumptive hyperphoria, determination of the right and left sursumduction may be employed for estimating the amount of real hyperphoria. Also in these cases may be employed the vertical line test recently described by me,[4] provided the patient can maintain bifixation of the line.

That in cases of occlusion hypertropia with heterophoria the entire deviation revealed by the cover test is that of real hyperphoria is not only a presumption but an erroneous presumption. This is obvious from the foregoing consideration and was one of the facts to which I pointed when I suggested the term presumptive hyperphoria.[4]

So far as I can ascertain, a satisfactory explanation of the anomaly under consideration has never been advanced. Bielschowsky, who has made a more extensive study of this subject than any other observer, stated,[5] after refuting other explanations: "The symptoms of double hyperphoria are due to alternating and intermittent excitations of both centers for vertical divergence." Even admitting the unproved assumption that such centers exist, this theory cannot be said to be satisfactory, since the intermittent excitations remain unexplained. Moreover, it does not explain why the deviation in question is always upward or why covering an eye should excite a center for vertical divergence. During the past five years I have studied with especial interest all such cases that have come under my observation. As a result of this study I have arrived at an explanation which I believe accords with all known physiologic, anatomic and pathologic facts.

I shall now attempt to detail in orderly sequence the considerations which lead to this explanation. Normally when one eye is covered it deviates slightly with respect to the other eye. When this deviation is considerable, it is commonly called heterophoria. When the eye is uncovered, bifixation (binocular fixation) is accomplished. The mechanism for this is commonly inaptly termed the "fusion" mechanism or faculty, although the descriptive term bifixation mechanism is obviously perfectly adequate. I have elsewhere discussed this mechanism to some extent.[4] For present purposes all that need be assumed in regard to it is that such a mechanism exists and that as concerns lateral deviations it is not thrown entirely out of action by the occlusion of one eye—it is still activated by the accommodation mechanism and usually also by the sense of distance. When the bifixation mechanism does not achieve bifixation, strabismus exists. Usually, when one eye alone is covered and the other eye changes its fixation from one distant object to another, the covered eye moves substantially concomitantly with its fellow. The same is true when the other eye alone is covered. What may be termed a monocular conjugate mechanism is acting when one eye is covered,

5. Bielschowsky, A.: Lectures on Motor Anomalies of the Eyes: Physiologic Introduction, Arch. Ophth. **12**:813 (Dec.) 1934.

and another when the other eye is covered. When both eyes are open, what may be termed a binocular conjugate mechanism is usually acting. If there is bifixation the conjugate movement is still more exact, but this precision may be due entirely to the bifixation mechanism. If, however, bifixation is prevented by means of a prism or is already lacking, i. e., if strabismus exists, usually both eyes still move substantially concomitantly unless there is paresis of one or more of the ocular muscles.

That a binocular and two monocular conjugate mechanisms exist and may be essentially different each from the other is evidenced by variations in the degree or character of nystagmus that can be elicited by means of the cover test in certain cases. Thus, cases exist in which conjugate nystagmus occurs when one eye alone is covered and not when the other eye alone is covered. These cases demonstrate that two monocular conjugate mechanisms exist, which may differ in certain respects. In certain cases of strabismus, when either eye alone is covered there is horizontal conjugate nystagmus, whereas when neither eye is covered there is no nystagmus or nystagmus of an entirely different kind, for instance, rotary nystagmus. It is to be noted that in these circumstances the bifixation mechanism cannot be concerned to any important extent, since strabismus exists. These cases demonstrate that a binocular conjugate mechanism exists which may differ from either or both of the monocular conjugate mechanisms. Recently I observed a case which showed that even a highly amblyopic eye can bring into action the binocular conjugate mechanism. In this case, although the squinting eye was amblyopic to the extent of $\frac{5}{200}$, marked horizontal conjugate nystagmus occurred when the amblyopic eye was covered and disappeared when it was uncovered. In this case it was also evident that the binocular conjugate mechanism was different from the monocular conjugate mechanism for the fixating eye. Additional and equally conclusive evidence of the existence of three such conjugate mechanisms is furnished by the cases of occlusion hypertrophia in which strabismus exists. For in many of these cases the deviation of the eyes with respect to each other markedly differs according to whether the right eye alone is covered, the left eye alone is covered or neither eye is covered.

The monocular and binocular conjugate mechanisms and the duction mechanism may together constitute one oculomotor mechanism, which is activated differently by different sensory conditions. In fact, I believe this actually to be the case. But for the purposes of this communication this question can be neglected.

Since normally when one eye is covered it moves conjugately with the other, it is clear that at some point in each of the direct ocular motor pathways for the right eye a conjugate pathway branches off and joins a suitable pathway for the left eye at a certain point. The pathway between these two points, since it is concerned only with the left eye

and carries only conjugate innervation, I shall term a left monocular conjugate pathway. The corresponding pathway leading to the right eye I shall term a right monocular conjugate pathway.

Possibly the monocular conjugate pathways are internuclear. Possibly also each may transmit innervation in either direction. For instance, the monocular conjugate pathway for the superior oblique muscle of one eye may serve also as the monocular conjugate pathway for the inferior rectus muscle of the other eye. But to assume this to be a fact requires the additional assumption that the single pathway may be unequally efficient in the two directions. To accord with usual concepts and with the present anatomic and physiologic knowledge, the assumptions may also be made that the binocular conjugate mechanism can utilize some or all of the monocular pathways and that the latter pathways are equally efficient for all voluntary innervation, however derived. For present purposes, however, none of these assumptions is essential.

Consider now any case in which, with neither eye covered, bifixation is absent or has been abolished. The nonfixating eye assumes a certain position with respect to its fellow. If this relative position as regards vertical deviation remains substantially unchanged for various positions of the fixating eye, obviously no important defect can exist in any of the pathways being used for voluntary upward or downward movement by the binocular conjugate system. If now when the nonfixating eye is covered it moves upward, one or more of its monocular conjugate pathways for vertical movement must be relatively defective in comparison with the binocular conjugate pathways. Since by my definition such an upward movement constitutes occlusion hypertropia, this type of hypertropia must be due to monocular conjugate excess involving one or both elevators, to monocular conjugate insufficiency involving one or both depressors or to both conjugate excess and conjugate insufficiency.

Since the deviation of occlusion hypertropia is upward, to answer the question at issue it is simply necessary to ascertain the muscle or muscles involved. Since occlusion hypertropia exists from early life, presumably, it is congenital. The superior oblique muscles are unique in regard to their anatomic relations and also in that the infranuclear pathways for their innervation cross not as do those of the other ocular muscles but in the ventral part of the midbrain. Moreover, these peculiarities were acquired late in phylogenetic development. Hence a congenital defect would be especially likely to exist in the conjugate pathways of the superior oblique muscle. As a matter of fact, in most of the cases, including those in the present series, that have come under my observation the change in deviation produced by covering the nonfixating eye was such as would have resulted from partial or complete relaxation of the superior oblique muscle. For generally the upward

deviation of the covered eye was associated with extorsion, was definitely increased when the eye was turned conjugately toward the nose and was relatively decreased when the fixating eye was elevated. In some cases, owing to slowness of the upward movement, the extorsion could be demonstrated only by the intorsion that occurred in the return movement when the eye was uncovered. It may be concluded, therefore, that in many cases occlusion hypertropia is due chiefly to monocular conjugate insufficiency of the superior oblique muscle.

The monocular conjugate insufficiency in cases of occlusion hypertropia might be mistaken for ordinary paresis of a depressor muscle were it not for the facts that the upward deviation disappears or alternates according to which eye is covered and disappears when neither eye is covered. These facts obviously do not accord with any usual concepts of oculomotor paresis.

The next question that arises is: Is the conjugate insufficiency complete or incomplete? The fact that the amount of upward deviation differs greatly in different cases would seem to indicate that the insufficiency is not always complete. In many cases the amount of upward deviation from the primary position is about 10 prism diopters, which is the amount usually found in cases of supposedly complete paralysis of a superior oblique muscle. Hence in such cases of occlusion hypertropia the conjugate defect is complete. It does not necessarily follow, however, that because the upward deviation is slight the conjugate defect is not complete, for a congenitally hypoplastic fourth nerve nucleus associated with complete conjugate insufficiency would obviously explain such deviation. Such a condition, if bilateral, would be manifested during binocular vision (i. e., when neither eye was covered) by evidences of so-called overaction of the inferior oblique muscles. Unfortunately, in my series of cases I did not investigate this question with sufficient care. However, in some of the cases this condition undoubtedly existed, and it is my impression, based on all the cases I have encountered, that "overaction of the inferior obliques" is common in cases of occlusion hypertropia. In 1 of my cases both inferior oblique muscles had previously been tenotomized by a colleague. In another case these muscles were later tenotomized by another surgeon. I am therefore strongly inclined to believe until further investigation proves otherwise that, at least in the cases of occlusion hypertropia in which there is "overaction of the inferior obliques," the monocular conjugate defect is complete and that in such cases differences in the amount of the deviation under cover are dependent on differences in the degree of nuclear hypoplasia.

Incidentally, the foregoing considerations suggest that "overaction of the inferior oblique" never really is such but is a condition due either to paresis of the superior oblique muscle or to hypoplasia of the nucleus of the fourth nerve.

Since the nucleus for the superior oblique muscle and that for the inferior rectus muscle on the same side probably are embryologically and also phylogenetically differentiated from the same single nucleus, it may be expected that the innervations of these nuclei will often be similarly defective. And as a matter of fact, in cases of occlusion hypertropia in which the upward deviation under cover is greater, and the extorsion less, than can be accounted for by relaxation of the superior oblique muscle alone, it seems evident that the monocular conjugate insufficiency concerns the conjugate pathways for both these muscles. In certain cases the inferior rectus muscle is chiefly concerned. In such cases the eye slightly intorts under cover, and the maximum upward deviation under cover exists when the deviating eye is down and somewhat out. In my present series the 2 cases in which occlusion hypertropia was strictly unilateral belonged in this class. No doubt in certain cases the possibility of hypoplasia of the nucleus for the inferior rectus muscle will need to be considered.

In some cases of alternating occlusion hypertropia the fixating eye intorts when a cover is applied to the other eye and extorts when the cover is removed. This means, of course, that in such cases the binocular conjugate mechanism does not employ direct innervation for at least one of the tortors of the fixating eye. For otherwise the eye would show no torsional movement when the other eye was uncovered. Since this communication is not chiefly concerned with the binocular conjugate mechanism, the possible explanations of these and analogous facts will not be discussed here. In this connection, however, it is to be noted that although, as has been shown, occlusion hypertropia is due to conjugate insufficiency, the amount of occlusion hypertropia may not exactly correspond to the amount of this insufficiency. For in certain cases the binocular conjugate mechanism may employ for the fixating eye one or more of the monocular conjugate pathways, and when neither eye is covered the position of the nonfixating eye relative to that of the fixating eye may in part depend on this fact.

The cases of occlusion hypertropia in which upward deviation of one eye persists even when this eye is not covered present interesting problems, which may require different answers in different cases. However, since the deviation of the nonfixating eye remains substantially unchanged when this eye is covered, there is evidently monocular conjugate insufficiency in all such cases. Assuming that uncovering this eye brings into action the binocular conjugate mechanism, then in the latter a defect or defects must exist exactly equivalent to the monocular conjugate insufficiency. But the assumption that when neither eye is covered the nonfixating eye continues to be innervated through its monocular conjugate mechanism would also explain these conditions.

This assumption is supported by the fact that in many cases of alternating occlusion hypertropia the poorer eye at times deviates upward even when not covered. A recent case observed by me seems to afford still stronger evidence in support of this assumption. In this case, whenever the patient (aged 3½ years) changed the fixation of his right eye from one object to another the left eye would quickly turn down to the level of the right, and as soon as the new fixation was accomplished by his right eye the left eye would, with somewhat less rapidity, deviate so far upward that the cornea was almost completely hidden by the upper lid. In an attempt to make the defect less conspicuous, I tenotomized the left superior rectus muscle. This reduced the upward deviation considerably, but when the patient changed his fixation with his right eye the left eye temporarily deviated below the level of the right (thus incidentally proving that the downward movement was not a fixation response on the part of the left eye). Evidently in this case the patient employed his relatively normal binocular conjugate mechanism while changing fixation from one object to another, and for his left eye his defective left monocular conjugate mechanism as soon as fixation was achieved. Whether or not in the cases of alternating occlusion hypertropia in which the monocular conjugate insufficiency is manifested with neither eye occluded the deviating eye provides the same useful vision that I have demonstrated for the deviating eye in ordinary cases of strabismus [6] I have not yet determined. I presume, however, that it does when the deviation concerned is habitual.

In this connection it is to be noted that the rapidity with which upward and downward movements of occlusion hypertropia occur varies in different cases and even at different times in the same case. The differences are probably due to variability in the conditions which cause a change from the monocular to the binocular conjugate mechanism and vice versa.

As to the conditions under which the binocular conjugate and the monocular conjugate mechanism are called into action, the following well known phenomena, which have been noted in cases of occlusion hypertropia, require consideration. If in a case of occlusion hypertropia the illumination reaching the retina of the affected eye is gradually decreased by a smoked glass wedge or by some other means, the eye, when the illumination becomes greatly reduced, will gradually deviate upward until, when the illumination is almost abolished, the eye attains the position it usually attains under an opaque screen. If the illumination is then gradually increased, the eye will gradually return to its usual position.

6. Verhoeff, F. H.: Anomalous Projection and Other Visual Phenomena Associated with Strabismus, Arch. Ophth. **19**:663 (May) 1938.

Bielschowsky [7] found that the eye would deviate upward if, instead of a smoked glass, a mirror was placed before it and a strong light from a window reflected into it. I have found that a ground glass will serve the same purpose. Bielschowsky also found, even in cases in which one eye was amblyopic, that a blurring lens placed before this eye would cause the latter to deviate upward. A convex spherical lens of high power, of course, definitely increases the retinal illumination.

In some cases of occlusion hypertropia (but not in all) if while one eye is deviated upward under cover the wedge is placed before the fixating eye, the covered eye, when the illumination becomes very low, gradually comes down and in cases of hypotropia or hypophoria may even reach a position below that of its fellow. This is known as the Bielschowsky phenomenon. In such cases the deviated eye may be made to resume its usual position by placing a blurring lens before the fixating eye. Evidently, therefore, neither of the two phenomena is dependent simply on reduction of retinal illumination. Obviously one of the most important factors in determining the attention value of a retinal image is its distinctness, and this is reduced by the introduction of a wedge, a ground glass, a mirror or a blurring lens before the eye. The foregoing observations, therefore, lead to the conclusion that the first phenomenon is dependent on marked decrease in the attention value of the retinal image in the deviating eye, and the Bielschowsky phenomenon, on an approach to equality in attention values of two contraocular retinal images when each is of low attention value. Hence it would seem that when the binocular conjugate mechanism is not acting it can be made to act by raising the attention value of the retinal image in the nonfixating eye and that the monocular conjugate mechanism of one eye can be made to act alone by greatly reducing the attention value of the retinal image in this eye. In both instances it is of course, assumed that the attention value of at least one retinal image is sufficient to maintain fixation.

But the problem is still more complex, because I have discovered by experiments on several patients with occlusion hypertropia that the effectiveness of an extremely weak retinal image or even of an imaginary image can be greatly raised by giving voluntary attention to it. Thus, in a recent case of marked alternating occlusion hypertropia with bifixation, I found that even when the luminosity of a retinal image in one eye was reduced almost to the point at which the image became invisible this eye would not deviate upward so long as the patient kept his attention on this image, and it appeared dark to him. As soon, however, as (at his own suggestion) he was told to look at the fixation object with

7. Bielschowsky, A.: Die einseitigen und gegensinnigen („dissoziierten") Verticalbewegungen der Augen, Arch. f. Ophth. **125**:491, 1930.

his other eye, although he was bifixating at this time, the eye with the darkened image deviated upward and he noted that the object he was observing became bright. (He had no diplopia at any time; in fact, I was unable to elicit diplopia in his case by any of the usual means.) In this case the Bielschowsky phenomenon could not be elicited, evidently because the darkened image always continued to attract undue attention. In 2 cases of strabismus with alternating occlusion hypertropia I found that voluntary attention to an imaginary object can cause the nonfixating eye to deviate upward while not covered. Thus, after instructing the patient to maintain fixation on a distant object after it could no longer be seen, I found that if the vision of the fixating eye was gradually obscured by a wedge the nonfixating eye, although not covered, deviated upward when the obscuration for the fixating eye was complete. Evidently, under these conditions, after the retinal image from the fixating eye became imaginary its effectiveness not only was continued by voluntary attention but was made so much stronger than before that it excluded or overpowered the usual effectiveness of the retinal stimuli from the nonfixating eye; that is to say, it abolished the action of the binocular conjugate mechanism and brought into action the monocular conjugate mechanism of the nonfixating eye.

In a case of left occlusion hypertropia with presumptive exophoria and no right occlusion hypertropia I made the analogous observation that the left eye, although not covered, deviated upward when the vision of the right eye was almost completely obscured by the wedge. Under these conditions the patient stated that she was using the right eye alone. It is interesting to note that as a result of this and similar tests the patient acquired the ability to bring into action at will the binocular conjugate mechanism or either of the monocular conjugate mechanisms. In other words, when so requested she could permit the right eye to deviate outward or the left eye to deviate outward and upward, or she could maintain fixation. I then found that after a few trials she could perform these same acts even when a large sheet of cardboard interposed close to her eyes obstructed her view of the fixation object. In a case of right occlusion hypertropia with strabismus in which the right eye was amblyopic to the extent of 20/200 (vision in left eye = 20/30 +) I made the observation that voluntary attention even to an imaginary object can prevent upward deviation of an eye while both eyes are covered. While the patient was fixating a distant lamp post, I requested her to continue looking at the place where the lamp post was when I covered both eyes. When I interposed a card before both eyes the right eye did not deviate upward with respect to the left until a few seconds later, when I uncovered only the left eye. Then the covered right eye deviated upward as usual. It is to be noted that in this case on neither retina was there

an actual image with attention value at the time there was no upward deviation of the covered right eye. Hence the voluntary attention to the unseen object must have stimulated the cortical representations of the two retinas just as if there had been a real image on each.

The foregoing observations and experiments are also of interest when considered in connection with certain purely sensory phenomena of binocular vision. For instance, as I have elsewhere pointed out,[8] attention value, so important in these experiments, is the controlling factor in replacement (so-called suppression). And I have experimentally demonstrated [9] that when the luminosity of one disparate retinal image is reduced greatly below that of the other stereoscopic depth effect is also reduced, although not nearly to a corresponding degree. It is well known that visual acuity does not begin to become appreciably reduced until the luminosity of the retinal images becomes very low. Further consideration of such phenomena is beyond the scope of this communication.

The total number of cases of occlusion hypertropia on which the conclusions arrived at in this communication were based was 42. Unfortunately, all of the patients could not be studied with equal completeness. To subject each patient to all the different tests employed would have required an expenditure of time too exorbitant for most patients to afford. The age of the youngest patient was 3½ years; that of the oldest was 45 years, and the ages of the others ranged from 8 to 40 years.

In 24 cases the occlusion hypertropia was associated with permanent strabismus. In 4 of these there was no cosmetically objectionable lateral deviation and no vertical deviation when occlusion hypertropia was not being manifested. In 17 cases there was originally esotropia of high degree, and in 13 of these cases operations for strabismus had been performed, which in 2 cases had resulted in exotropia. Two cases, originally of esotropia, had also become cases of exotropia, 1 as a result of development of myopia and the other as a result of marked decrease in hypermetropia. There were only 3 cases originally of exotropia. In 9 cases there was amblyopia ex anopsia (least marked, 20/50; most marked, 1/200). In 1 case vision in one eye was reduced by a congenital macular lesion to perception of hand movements. In 3 cases, all originally cases of esotropia, there was pure rotary nystagmus when neither eye was covered. In 1 of these cases there was horizontal nystagmus when one eye was covered. In 2 cases there was nystagmus only when

8. Verhoeff, F. H.: A New Theory of Binocular Vision, Arch. Ophth. **13**: 151 (Feb.) 1935.

9. Verhoeff, F. H.: Effect on Stereopsis Produced by Disparate Retinal Images of Different Luminosities, Arch. Ophth. **10**:640 (Nov.) 1933.

one eye was covered, in 1 case vertical and in the other horizontal. In 1 case there was slight horizontal nystagmus when neither eye was covered.

Of the 18 cases of occlusion hypertropia without permanent strabismus, i. e., cases in which bifixation existed, there was a history or other evidence of previously existing esotropia in 10 and of previous occasional exotropia in 3. Operations for strabismus had previously been performed in 8 cases. At the time of the examination for occlusion hypertropia there was no important horizontal deviation under cover in 11 cases. Five of these were cases in which original esotropia had been overcome by operations. In 2 cases there was persisting esotropia for distance and bifixation for near vision. In 1 case, originally a case of exotropia, operation had resulted in esotropia for distance and bifixation for near vision. In 4 cases there was presumptive exophoria at the time of examination. In 1 of these, when the patient was 10 years old, there had been esophoria due to high grade hypermetropia, and correcting glasses had finally caused the presumptive exophoria at the age of 15 years. In another there had been originally esotropia also, and the presumptive exophoria observed at the age of 22 years resulted from the development of myopia. In the other 2 cases an original "exophoria" had persisted. In 4 cases there was monocular amblyopia (1 case, 20/50; 2 cases, 20/100; 1 case, 20/200). In 2 of these there was no marked horizontal deviation under cover; in 1 there was originally esotropia and later presumptive exophoria, and in the other there was esotropia for distance. It is remarkable that in all 4 cases the kinetic test [10] showed excellent stereopsis in spite of the amblyopia.

In 3 of the cases in which there was bifixation there was nystagmus. In 2 of these the nystagmus was horizontal and occurred only when one eye was covered. In the other case it was horizontal when one eye was covered and rotary during bifixation.

It is noteworthy that among all the 42 cases there were no more than 5 cases in which occlusion hypertropia could be regarded as an isolated anomaly. In all the others it was originally associated with strabismus or marked "heterophoria." In 2 cases in which there was no amblyopia the occlusion hypertropia was strictly unilateral. One was a case of exophoria; the other, of exotropia.

It is noteworthy also that in 9 of the 42 cases there was nystagmus. In 4 of these the nystagmus was rotary, a fact possibly of considerable significance, since occlusion hypertropia chiefly concerns the superior oblique muscles. However, the importance of this fact cannot be fully evaluated until more is known of the mechanism of nystagmus.

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10. Verhoeff, F. H.: A Kinetic Test for Stereoscopic Vision, Arch. Ophth. **15**:833 (May) 1936.

From an analysis of this series of cases of occlusion hypertropia it may be concluded that the condition is generally associated with one or more other defects in the ocular motor mechanisms.

TREATMENT

In the great majority of cases the correction of occlusion hypertropia is not a problem, since it is not manifested when neither eye is occluded. However, it is often associated with strabismus or heterophoria, which may require correction. In the presence of strabismus the defects other than occlusion hypertropia are obvious and may be corrected by operation as usual. But in the cases of occlusion hypertropia with heterophoria the problem is not so simple, for, as has been indicated, the tests employed may throw the binocular conjugate mechanism out of action and thus render the determination of the heterophoria difficult. The cover test, of course, always does so. In such cases the presumptive laterophoria should be corrected first. Then the amount of real hyperphoria should be estimated by the methods already referred to. If feasible, the estimated hyperphoria should then be corrected by prisms. The final test of the correction, as in all other cases of heterophoria, is the improvement in visual acuity and comfort experienced by the patient.

As to the treatment in the unusual cases in which occlusion hypertropia is frequently or constantly manifested with neither eye occluded, my experience is too limited to warrant basing any conclusions on it. Certain theoretic considerations, however, seem obvious in this connection. It would seem that the visual acuity of the deviating eye should be made as high as possible by careful correction of refractive errors, in the hope that this procedure may bring into action the binocular conjugate mechanism. In the cases of young persons with amblyopia of the deviating eye, prolonged occlusion of the other eye should be tried. Operation on one eye, if it resulted in bringing into action the binocular conjugate mechanism, would be disastrous, since then an actual marked hyperphoria or hypertropia would exist. If in a case of alternating occlusion hypertropia the occlusion hypertropia of one eye were corrected to any extent by operation, then when this eye fixated the upward deviation of the other eye would be greater than ever, for it would have actual hypertropia in addition to occlusion hypertropia. To prevent the eye which had been operated on from fixating, it would be necessary either to employ a blurring glass before it or to teach the patient never to fixate with it.

The question arises whether monocular conjugate insufficiency of any muscles other than the superior oblique and inferior rectus muscles ever occurs; in other words, whether occlusion hypotropia, occlusion esotropia or occlusion exotropia may occur. As has been stated, I have

never encountered a case of "katatropia" (occlusion hypotropia), although Stevens implied that such cases occur. Bielschowsky [11] made no mention of such a case. As regards the lateral rectus muscles, if there were bifixation but monocular conjugate insufficiency of one lateral rectus muscle this would be manifested in the cover test as "esophoria" or "exophoria," which would be greater when the cover was applied to one eye than when applied to the other eye. The cover test sometimes reveals such a condition, but it is generally explained on the assumption that in monocular vision the convergence mechanism is activated more strongly from one eye than from the other. If a lateral deviation under cover is found to be nonconcomitant, paresis of the muscle concerned is assumed. In some cases of esotropia I have observed that the esotropia is increased at times by covering the deviating eye. Hence it is possible that monocular conjugate insufficiency of one or more of the lateral rectus muscles may occur without being recognized. An attempt, therefore, should be made to investigate this problem by suitable experiments, for example, subjecting the patient to conditions which elicit the Bielschowsky phenomenon.

SUMMARY AND CONCLUSIONS

The terms alternating hyperphoria, double hyperphoria, and alternating hypertropia are misnomers and should be abandoned. For the condition which gave rise to their use the term occlusion hypertropia is suggested.

Three conjugate mechanisms can be differentiated, two monocular and one binocular.

Occlusion hypertropia is due to congenital monocular conjugate insufficiency and may be unilateral or bilateral. This conjugate insufficiency may concern the superior oblique muscle, the inferior rectus muscle or both. Usually it concerns chiefly the superior oblique muscle.

Occlusion hypertropia is usually associated with other ocular motor defects which are probably congenital, notably esotropia or "esophoria." Not infrequently it is associated with nystagmus. Often it is associated with congenital hypoplasia of one or both fourth nuclei, producing the effect of so-called overaction of one or both of the inferior oblique muscles.

It is important to recognize and allow for occlusion hypertropia in deciding on the treatment, operative or otherwise, to be employed in cases of strabismus or "heterophoria."

The question of the possible occurrence of monocular conjugate insufficiency of the lateral rectus muscles should be investigated.

11. Footnotes 5 and 7.

BIOCHEMISTRY OF THE LENS

XIII. PRODUCTION OF LENS OPACITIES BY INJECTION OF HYPERTONIC SOLUTIONS

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AND
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In the passage of nutrient material from the blood to the lens two barriers must be traversed, namely, the ciliary processes (blood-aqueous barrier) and the lenticular capsule (aqueous-lens barrier). The same two barriers in reverse order oppose the removal of waste products of lens metabolism. Concentration gradients exist across each of these barriers, gradients that change continuously. Thus, there is operative at all times a dynamic equilibrium of osmotic forces between the lens and the aqueous on the one hand and between the aqueous and the blood on the other. Not only is there a continuous interchange of blood and waste products, but there is a simultaneous and delicately balanced alteration of the water content. For example, a meal rich in carbohydrates is ingested, which increases the dextrose content of the blood. Since the concentration of dextrose in the blood is then higher than that in the aqueous, a higher osmotic pressure is found in the former fluid and fluid is drawn from the aqueous into the blood. The removal of water from the aqueous causes a momentary decrease in the supporting pressure of the lens, enabling it to expand and causing increased permeability of the capsule. This in turn may allow the escape of minute amounts of fluid and dissolved constituents. As the water is being drawn from the aqueous into the blood, dextrose is at the same time diffusing from the blood into the aqueous. This increases the concentration in the latter fluid to a level above that in the lens. Fluid is then removed, and the lens tends to shrink. Simultaneously with these changes, the waste products of lens metabolism are making their way to the blood and producing changes similar in nature but opposite in direction to those already described. Thus, the lens acts as a delicate osmometer, never remaining static but changing constantly in volume, shape and content. Normally these alterations do not interfere with vision, but in pathologic states the balance may be upset to such a degree that refractive changes occur, finally with death of the lens.

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In this connection it is significant that transient refractive changes associated with the heightened dextrose content of the aqueous humor in cases of diabetes have long been noted. More severe diabetic conditions may result in cataract. Duke-Elder [1] has suggested that these opacities are caused by severe alterations of the fluid equilibrium of the lens and the aqueous resulting from osmotic derangements.

Experimentally, there has been a great deal of work to show that widespread changes of the lens may result from alteration of the crystalloid content of the ocular fluids. Kunde [2] was the first to observe that lenses dropped into hypertonic solutions of sodium chloride or sugar became turbid but rapidly regained their transparency when the solution was replaced by distilled water. Deutschmann [3] reported that opacities resulted when fresh sheep or pig lenses were dropped into 1.75 per cent sodium chloride solutions. A cataract was produced with 20 per cent dextrose solution comparable to that obtained with 5 per cent sodium chloride. With 5 per cent dextrose a slight cloudiness resulted after a long period, and with 2 per cent dextrose no change was observed. Deutschmann also reported the decrease in weight of the lens following such immersion. This in vitro production of salt cataract was repeated and extended by numerous workers, including Heubel,[4] Michel,[5] Hess,[6] Burge,[7] Bergami,[8] Löwenstein and Haurowitz,[9] Fischer [10] and others. An excellent review of the early investigations was given by Hess [6] and of the more recent work by von Szily.[11]

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1. Duke-Elder, W. S.: Changes in Refraction in Diabetes Mellitus, Brit. J. Ophth. **9**:167-186, 1925.

2. Kunde, F.: Ueber Wasserentziehung und Bildung vorübergehender Katarakte, Ztschr. f. wissensch. Zool. **8**:466, 1857; cited by Deutschmann.[3]

3. Deutschmann, R.: Untersuchungen zur Pathogenese der Katarakt, Arch. f. Ophth. **23**:112-147, 1877.

4. Heubel, E.: Ueber die Wirkung wasserentziehende Stoffe, insbesondere auf die Kristallinse, Arch. f. d. ges. Physiol. **20**:114-188, 1879.

5. Michel: Ueber natürliche künstliche Linsentrubung, in Festschrift zur dritten Sæcularfeier der Alma Julia Maximiliana gewidmet von der medicinischen Facultät Würzburg, Leipzig, F. C. W. Vogel, 1882; cited by Hess.[6]

6. Hess, C.: Pathologie und Therapie des Linsensystems, in Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1911, vol. 6, pt. 2, chap. 9, p. 253.

7. Burge, W. E.: The Production of Cataract, Arch. Ophth. **47**:12-28, 1918.

8. Bergami, G.: Azione delle basse temperature sulla lente cristallina, Atti Accad. naz. d. Lincei **6**:117, 1927; cited by von Szily.[11]

9. Löwenstein, A., and Haurowitz, F.: Experimentelle Untersuchungen über das Verhalten den Rinderlinsen bei Veränderung des umgebenden Mediums, Arch. f. Ophth. **122**:654-660, 1929.

10. Fischer, F. P.: Wasserbindung, Durchsichtigkeit, und Durchlässigkeit der Linse, Arch. f. Augenh. **108**:80-125, 1933.

11. von Szily, A., in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie, Berlin, Julius Springer, 1937, vol. 11, pt. 3.

In addition to these in vitro studies, cataracts have been produced by the in vivo administration of sodium chloride and other crystalloids through various routes. The earliest report of such a procedure again was that by Kunde.[2] Kunde injected subcutaneously into frogs sodium chloride, sodium nitrate and dextrose and was able in each instance to produce turbidities of the lens. With mammals Kunde had less success. He was able to produce a slight lenticular opacity only in young cats by subcutaneous injection of sodium chloride. He explained the salt cataract on the basis of removal of water from the lens. Köhnhorn's findings [12] gave support to this hypothesis, since he demonstrated that frogs placed in a bell jar with calcium chloride also became cataractous. Opposing this view were Mitchell [13] and Guttmann.[14] The former was unable to produce cataracts in frogs by generalized dehydration. He placed the frogs without water in a bell jar at 75 to 88 F. until death (five to six days) without observing any signs of cataract. The latter investigator injected large doses of calcium chloride—a very hygroscopic compound—with no observable changes in the lens.

Richardson [15] produced cataractous lenses by injecting dextrose, sucrose and lactose subcutaneously into frogs. In 1 instance he was successful in obtaining cataracts in the rabbit by injecting "one ounce of cane sugar syrup" intraperitoneally and repeating the injection after ten hours. Introduction of crystalline sodium chloride into the dorsal lymph sac of the frog resulted in bilateral cataracts.[3] Richardson was also the first to produce cataract by injecting "syrup" directly into the anterior chamber of a sheep's eye. This finding was extended by Deutschmann,[3] Panico [16] and Collevati.[17] In addition to these routes of administration, many others have been employed with varying degrees of success. Thus, Manca and Ovio [18] produced cataracts in frogs by instillation of sodium chloride, potassium chloride, dextrose, etc., into the conjunctival sac; Kunde [2] obtained cloudiness of the lens by oral or rectal injection of salts in cats; and Salffner [19] in a single instance

12. Köhnhorn, C.: De cataracta aquae inopia effecta, Inaug. Dissert., Greifswald, F. G. Kunike, 1858; cited by Deutschmann.[3]

13. Mitchell, S. W.: On the Production of Cataracts in Frogs by the Administration of Sugar, Am. J. M. Sc. **39**:106-110, 1860.

14. Guttmann, P.: Experimentelle Untersuchungen über die Wirkung der Kali- und Natronsalze, Berl. klin. Wchnschr. **2**:367-370, 1865.

15. Richardson: Report Before the Medical Society of London, M. Times & Gaz. **1**:319, 1860.

16. Panico, E.: Cataratta da cloruro de sodio, Ann. di ottal. e clin. ocul. **57**: 613, 1929; cited by von Szily.[11]

17. Collevati, cited by von Szily.[11]

18. Manca, G., and Ovio, G.: Studio intomo alla cataratta artificiale, Arch. di ottal. **6**:69, 1898; cited by von Szily.[11]

19. Salffner, O.: Zur Pathogenese des Naphthalinstares, Arch. f. Ophth. **59**: 520-552, 1904.

observed opacities in a rabbit following intravenous injection of a salt mixture. Selenkowski [20] injected hypertonic saline solution into the lens itself, and a cataract resulted. Erlanger [21] obtained similar results by introducing sodium chloride and barium salts into the eye iontophoretically.

The bulk of these investigations suggested that turbidity of the lens is produced by a generalized effect depending on the hypertonicity of the solution rather than on a specific action of the compound or ion injected. To test this and to gain more information on the subject, a variety of relatively innocuous compounds were injected intravenously into dogs and rats. The list of cataractogenic agents was markedly increased by our findings. In addition, data concerning the changes in the chemical composition of the body fluids and the ocular tissues seemed essential to a better understanding of the process. These are reported in a later section. Finally, a comparison was attempted of the chemical alterations between lenses made cataractous by injection of hypertonic solutions and lenses made opaque by other means. It has long been known that the cataractous lens gives a negative nitroprusside reaction, indicating an absence of sulfhydryl groups, chiefly glutathione.[22] This disappearance has been noted prior to any positive ophthalmoscopic abnormalities in cases of galactose cataract.[23] A lowering of the ascorbic acid content is usually a concomitant finding.[24] The potassium content decreases as the lens ages and may drop to very low levels in certain cataractous lenses.[25] It has been shown that the lenticular protein breaks down into simpler nitrogenous units as the

20. Selenkowski, J.: Zur Frage der experimentellen Stare im Zusammenhang der künstlichen Reifung unreifer oder unvollständiger Stare, Russk. oftal. **3**:613, 1925; cited by von Szily.[11]

21. Erlanger, G.: Katarakterzeugung durch Iontophorese: Experimentelle Studien, Klin. Wchnschr. **7**:2391-2392, 1928.

22. Reis, W.: Ueber die Cysteinreaktion der normalen und pathologisch veränderten Linsen, Arch. f. Ophth. **80**:588-598, 1911. Jess, A.: Zur Chemie der Catarakt senilis, Arch. f. Augenh. **21**:259-266, 1912. Tassman, I. S., and Karr, W. G.: Glutathione in the Crystalline Lens, Arch. Ophth. **2**:431-436 (Oct.) 1929.

23. Bellows, J. G.: Biochemistry of the Lens: Influence of Vitamin C and Sulfhydryls on the Production of Galactose Cataract, Arch. Ophth. **16**:762-769 (Nov.) 1936. Bellows, J. G., and Rosner, L.: Studies on Galactose Cataract, Am. J. Ophth. **20**:1109-1114, 1937.

24. Rosner, L.; Farmer, C. J., and Bellows, J. G.: Biochemistry of the Lens: XII. Studies on Glutathione in the Crystalline Lens, Arch. Ophth. **20**:417-426 (Sept.) 1938.

25. Burge, W. E.: Analyses of the Ash of the Normal and the Cataractous Lens, Arch. Ophth. **38**:435-450, 1909. McKay, G.; Steward, C. P., and Robertson, J. D.: A Note on the Inorganic Constituents of Normal and Cataractous Human Crystalline Lenses, Brit. J. Ophth. **16**:193-201, 1932.

cataract progresses.[26] This is manifested in a decreased protein content and an increased nonprotein nitrogen content. None of these alterations were observed in the lenses made cataractous by injection of hypertonic crystalloid solutions.

EXPERIMENTAL DATA

A total of 46 young dogs and over 200 albino rats were employed. The test solutions were injected intravenously at a constant rate. In the rat 2 to 3 drops and in the dog 10 to 15 drops per minute was injected into the femoral vein. Blood was withdrawn for analysis from the opposite femoral vein or from the jugular vein in the dog and from the tail of the rat. Spinal fluid was aspirated by suboccipital puncture. All solutions injected were approximately isotonic with 10 per cent sodium chloride. Because of the extreme toxicity of these solutions in such high concentrations, rats rarely survived more than two hours and dogs more than six hours (average, five hours and three minutes). The lethal dose (for dogs) of sodium chloride given at this concentration and rate ranged from 2.22 to 9.33 Gm., with an average of 5.67 Gm. per kilogram. Duke-Elder[27] has discussed the relation of lethal doses of hypertonic saline solution to the concentration

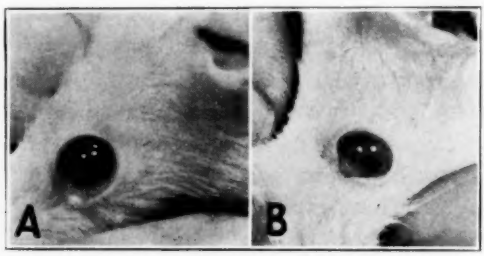

Fig. 1.—*A*, normal eye prior to injection. *B*, cataractous eye after injection of 10 per cent sodium chloride intravenously for ninety minutes at a rate of 2 to 3 drops per minute. Note that the central area is still relatively clear.

of the solution and its rate of injection. He found 1.5 Gm. per kilogram to be fatal to cats when injected at the rate of 1 cc. of a 30 per cent solution per minute. Our experiments indicate that almost four times this amount can be given to dogs if the concentration is reduced to 10 per cent.

Lenticular opacities were observed after administration of sodium chloride, sodium sulfate, lithium chloride, sodium lactate, arabinose, glycerin, ethylene glycol, ethyl alcohol, xylose, galactose and aminoacetic acid. The effects with a number of other compounds were inconclusive because of the early death of the animal. In some instances changes could be seen within twenty to thirty minutes. In the rat, within this period one can see with the naked eye accentuation of the markings of the suture lines and a gradual progressive cloudiness. This may become so marked that the ophthalmoscopically induced fundus reflex becomes gradually dimmed. The opacity shown in figure 1 *B* is typical. This photograph was taken ninety minutes after injection of 10 per cent sodium chloride was begun.

26. Jess, A.: Beiträge zur Kenntnis der Chemie der normalen und der pathologisch veränderten Linse des Auges, Ztschr. f. Biol. **61**:93-142, 1913. Kulik, J.: Zur Pathologie menschlicher Stare, Arch. f. Augenh. **102**:657-667, 1930.

27. Duke-Elder, W. S.: The Reaction of the Intraocular Pressure to Osmotic Variations in the Blood, Brit. J. Ophth. **10**:1-29, 1926.

Examined under the slit lamp, the capsule of the lens appeared perfectly clear. However, the subcapsular cortex was cloudy. This cloudiness was greatest about the Y suture lines, so that they are thrown into sharp relief. As the injection of hypertonic solutions continued, separation of the lens fibers and occasional water fissures and vacuoles appeared. Histologic study of the rat lenses showed nothing abnormal. The vacuoles in the capsular epithelium in frogs, described by Deutschmann,[3] were never seen by us.

In the few specimens of dog lenses studied we observed fissures in the cortex, in the area immediately surrounding the nucleus. These were not seen in the control eyes. However, the lenses examined were too few to enable us to state categorically that these changes were not artefacts.

In several instances the injections were discontinued after undoubted opacity had developed but before the death of the animal. In these cases rapid regression of the cataract was seen, with a return to the normal transparent condition within several days.

In addition to these changes in the lens, the eyeball became markedly softer during the injection. That these changes were due to the removal of water, as was stated by Hertel,[28] can be seen from table 1.

TABLE 1.—*Loss in Weight of Eyeball Following Intravenous Injection of Ten Per Cent Sodium Chloride Solution*

Average Duration of Injection, Hours	Original Weight of Eye, Gm.	Weight of Other Eye After Injection, Gm.	Loss of Weight, Gm.	Percentage Loss
5.05	4.060	3.697	0.363	8.94

At the start of the experiment one eye was enucleated, dissected free from adherent tissue, dried on filter paper and weighed. Immediately after the death of the animal the remaining eye was removed and similarly treated. A loss in weight of 8.94 per cent was noted. This loss was due presumably to the removal of water from the eyeball because of the raised osmotic pressure of the blood. The loss in weight of the dogs' eyes (8.94 per cent) in the average period of five hours compares with the loss in weight of a rabbit's eye (8.38 per cent in forty-two minutes and 3.02 per cent in eighteen minutes [29]). From table 2 it can be seen that this loss of water is not confined to any individual tissue of the eye. The lens showed the greatest percentage loss, with the retina, cornea, sclera and vitreous following, in that order.

In an attempt to correlate the morphologic changes in the eye with the chemical changes induced by the hypertonic saline solution, the fate of the injected sodium chloride was followed. Changes in the sodium and in the chloride content of the serum, spinal fluid and body tissues were determined, as well as changes in the various tissues of the eye. The sodium content of the aqueous humor, blood and spinal

28. Hertel, E.: Experimentelle Untersuchungen über die Abhängigkeit der Augendrucks von der Blutbeschaffenheit, Arch. f. Ophth. **88**:197-229, 1914.

29. Calculated from the data of Hertel.[28]

fluid was determined by the method of Butler and Tuthill,[30] and the chloride content, by Van Slyke's procedure.[31] The various ocular tissues were dissected free of extraneous material, dried at 105 to 110 C. for forty-eight hours and then analyzed for sodium and chloride according to the procedure of Cullen and Wilkins.[32] As can be seen from table 2, the original sodium content of the sclera and of the cornea is highest, with the vitreous and retina next and the lens by far the poorest. After injection of sodium chloride the percentage increase of sodium is roughly in the same order: cornea, 65 per cent; vitreous, 43 per cent; sclera, 41 per cent; retina, 40 per cent, and lens, 18 per cent. For chloride the original values in descending order follow: sclera, vitreous, cornea, retina and

TABLE 2.—*Penetration of Sodium Chloride into the Ocular Tissues*

Tissue	Per Cent Water	Mg. per 100 Gm. Tissue		mEq. per 100 Gm. Tissue		Mg. per 100 Gm. Water		mEq. per 100 Gm. Water	
		Na^+	Cl^-	Na^+	Cl^-	Na^+	Cl^-	Na^+	Cl^-
Lens:									
Before	63.97 ± 0.49	64.1 ± 7.7	36.2 ± 2.2	2.79 ± 0.33	1.02 ± 0.07	100.0 ± 12.9	60.5 ± 4.8	4.35 ± 0.56	1.71 ± 0.06
After	61.29 ± 0.47	73.2 ± 8.2	57.0 ± 10.0	3.18 ± 0.36	1.61 ± 0.21	118.1 ± 12.9	95.4 ± 11.7	5.13 ± 0.56	2.69 ± 0.33
Vitreous:									
Before	98.87 ± 0.02	346.4 ± 5.4	461.3 ± 3.8	15.06 ± 0.24	13.01 ± 0.11	350.8 ± 5.5	470.2 ± 3.9	15.29 ± 0.24	13.26 ± 0.11
After	98.44 ± 0.02	496.8 ± 8.5	680.3 ± 9.3	21.59 ± 0.38	19.18 ± 0.26	504.7 ± 10.4	692.6 ± 9.4	21.95 ± 0.45	19.53 ± 0.27
Retina:									
Before	85.46 ± 0.38	278.8 ± 6.1	296.4 ± 5.9	12.12 ± 0.26	7.60 ± 0.17	329.8 ± 8.1	317.1 ± 6.5	14.34 ± 0.35	8.94 ± 0 19
After	85.36 ± 0.27	391.5 ± 9.0	427.1 ± 16.8	17.02 ± 0.39	12.04 ± 0.47	463.1 ± 10.8	518.4 ± 21.0	20.13 ± 0.49	14.62 ± 0.59
Cornea:									
Before	76.15 ± 0.40	313.6 ± 21.4	323.7 ± 8.3	13.63 ± 0.93	9.13 ± 0.23	419.2 ± 28.8	424.9 ± 11.0	18.23 ± 1.25	11.98 ± 0.31
After	74.53 ± 0.39	507.4 ± 34.1	541.8 ± 12.5	22.06 ± 1.48	15.28 ± 0.35	693.0 ± 46.2	719.9 ± 19.5	30.13 ± 2.01	20.30 ± 0.54
Sclera:									
Before	66.37 ± 0.68	278.0 ± 16.4	324.3 ± 7.3	12.09 ± 0.71	9.14 ± 0.20	426.7 ± 27.0	478.1 ± 11.5	18.53 ± 1.17	13.48 ± 0.32
After	65.75 ± 0.34	397.7 ± 18.1	542.4 ± 18.1	17.96 ± 0.79	15.29 ± 0.52	604.4 ± 26.4	829.9 ± 31.8	26.28 ± 1.15	23.40 ± 0.90

lens. The percentage increase after injection were: sclera, 74 per cent; cornea, 69 per cent; lens, 57 per cent; retina, 47 per cent, and vitreous, 43 per cent. Owing to the fact that the concentration of chloride in the lens is far lower than in any other tissue, this percentage increase is misleading. The absolute

30. Butler, A. M., and Tuthill, E.: An Application of Uranyl Zinc Acetate Method for the Determination of Sodium in Biological Material, J. Biol. Chem. **93**:171-180, 1931.

31. Van Slyke, D. D.: The Determination of Chlorides in Blood and Tissues, J. Biol. Chem. **58**:523-529, 1923.

32. Cullen, G. E., and Wilkins, W. E.: Electrolytes in Human Tissue: I. The Digestion of Tissue and Other Biological Material and the Subsequent Determination of Various Electrolytes, J. Biol. Chem. **102**:403-412, 1933.

increase in chlorides of the lens (36 to 57 mg. per hundred grams) is actually less than one-fifth that of any other tissue.

A comparison of our findings on the dog with those on other animals is made in table 3. The values we obtained were, in general, higher than those found by other workers. The values varied somewhat with the different species, the ocular tissues of the dog having the highest concentrations and those of the cow the lowest. Despite these variations in absolute amounts, the relative concentrations of the different tissues were the same regardless of species. Thus, the lens invariably contained the least sodium and chloride of any tissue, with the retina, sclera, cornea and vitreous following in ascending order.

As can be expected, the injection of such large quantities of electrolytes raised the osmotic pressure of all the body fluids. This is shown graphically in figure 2. The osmotic pressure was determined by the usual cryoscopic method. Spinal

TABLE 3.—*Species Variations in the Sodium Chloride Content of Ocular Tissues*

	Rabbit		Swine †		Cow †		Ox †		Dog		Horse	
	Mg. per 100 Gm.		Mg. per 100 Gm.		Mg. per 100 Gm.		Mg. per 100 Gm.		Mg. per 100 Gm.		Mg. per 100 Gm.	
Tissue	Na^+	Cl^-	Na^+	Cl^-	Na^+	Cl^-	Na^+	Cl^-	Na^+	Cl^-	Na^+	Cl^-
Vitreous	...	...	350	397	317	382	322	396	346	461	...	...
Cornea	...	...	288	330	247	225	263	260	314	324	...	...
Sclera	...	...	175	276	160	213	183	224	278	324	...	...
Retina	...	...	170	150	142	154	147	155	279	296	...	...
Lens	...	...	116	116	66	61	69	46	64	36	...	...
Aqueous	317*	385#	...	...	337*	434*	339‡	437‡	314§ 310	402§ 441	362‖	457¶

* Baurmann, M.: Vergleichende Messungen des Elektrolytgehaltes von Serum, Serumultrafiltrat und Kammerwasser, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. (1928) **47**: 157-169, 1929; cited by Krause, A. C.: Biochemistry of the Eye, Baltimore, Johns Hopkins Press, 1934.

† Fischer, F. P.: Der Mineralbestand des Auges, Arch. f. Augenh. **107**: 295-318, 1933.

‡ Tron, E.: Chemische Untersuchungen die Natur der intraokulären Flüssigkeiten: I. Trockensubstanz, Kalium und Calcium im Kammerwasser, Glaskörper, und Blutserum der Ochsen und Pferdes, Arch. f. Ophth. **117**: 677-692, 1926.

§ Gaedertz, A., and Wittgenstein, A.: Ueber den Kationengehalt des Kammerwassers im lebendes Warmblüterauge, Arch. f. Ophth. **118**: 738-744, 1927.

¶ Winternitz, R., and Stary, Z.: Zur Anionpermeabilität der Blut-Kammerwasserschranke, Ztschr. f. d. ges. exper. Med. **89**: 540-550, 1933.

‖ Stary, Z., and Winternitz, R.: Zur Chemie des Kammerwassers, Ztschr. f. physiol. Chem. **212**: 215-233, 1932.

Duke-Elder, W. S.: Text Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1933, vol. 1, p. 431.

fluid was aspirated only at the time of death, to obviate changes due to the formation of a plasmoid type of fluid. Values for normal spinal fluid were obtained from the literature.[33] The osmotic pressure of the blood rose from 34.5 milliosmoles[34] per hundred grams of water before injection to 78.2 milliosmoles at death. This rise paralleled the increase of the sodium and chloride content of the blood. At death the concentration of sodium was 209 per cent, of chloride 207 per cent and of the osmotic pressure 221 per cent of the original. The electrolyte content and osmotic pressure of the spinal fluid and the aqueous humor showed a less marked rise than that of the blood. At death the concentration of sodium in the spinal fluid was 145 per cent and that of chloride 161 per cent;

33. Shohl, A. T.: Mineral Metabolism, New York, Reinhold Publishing Company, 1939.

34. The milliosmoles, or osmotic equivalents per hundred grams of water, can be calculated from the freezing point data as follows:[33]

$$\frac{\text{Freezing point depression}}{1.86} \times \frac{100}{\%\ \text{water (decimal)}}$$

the osmotic pressure was 161 per cent of the original. The sodium content, chloride content and osmotic pressure of the aqueous humor rose to 156, 159 and 153 per cent (estimated) respectively. It is interesting to note that the hemoglobin decreased as the sodium and chloride increased, indicating an increased blood volume. The sharpest rise in the blood electrolytes (fourth to sixth hour) corresponded with the steepest drop of the hemoglobin concentration. The increased blood volume resulting from this hemodilution invariably evoked an intense diuresis. Because of this continuously changing blood volume, it was necessary to make allowances for the increased water content of the blood in calculating the electrolytes and osmotic pressure per hundred grams of water.

Table 4 indicates that the increase in sodium and chloride was shared by all the body tissues. Considerable variation was found from dog to dog, as can be seen by the probable error of the values reported. This may have been due to a number of factors, such as differences in water content, removal of different parts of the organ for analysis and variations in age. Nevertheless, the increase

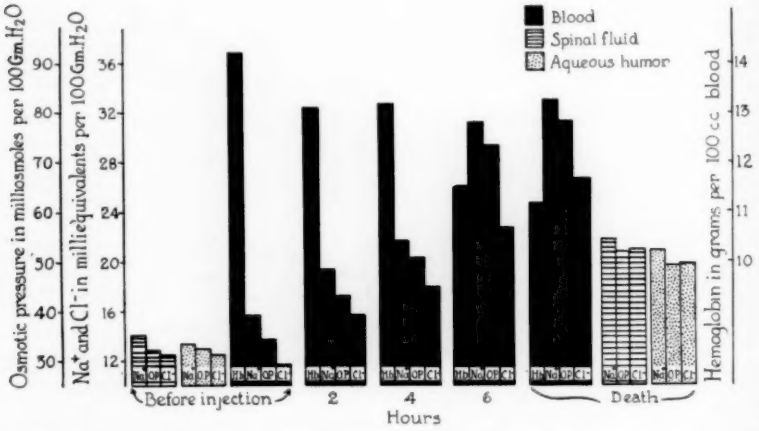

Fig. 2.—Chemical studies of the blood, the aqueous humor and the spinal fluid during injection of 10 per cent sodium chloride. The original values for spinal fluid were taken from Shohl [33] and those for aqueous humor from Krause (Krause, A. C.: Biochemistry of the Eye, Baltimore, Johns Hopkins Press, 1934). The osmotic pressure of the aqueous humor at death was estimated.

in electrolyte content was striking and in most cases was even greater than that found in the tissues of the eye.

The lens was analyzed before injection and at the time of death for potassium, ascorbic acid, glutathione and nonprotein nitrogen, since each of these constituents has been reported as changing with the development of cataract.[35] The potassium content was determined by the Kramer and Tisdall [36] method after the lens had been treated according to the directions of Cullen and Wilkins.[32] The lens was analyzed for ascorbic acid and glutathione by the procedure of Rosner, Farmer and

35. Footnotes 23, 24, 25 and 26.

36. Kramer, B., and Tisdall, F. T.: A Clinical Method for the Determination of Potassium in Small Amounts of Serum, J. Biol. Chem. **46**:339-349, 1921.

Bellows.[24] The nonprotein nitrogen content was found by precipitating the proteins of the lens with 10 per cent trichloroacetic acid. An aliquot portion of the supernatant liquid (after filtration through no. 41 Whatman's paper) was then digested, nesslerized and compared colorimetrically by the Koch-McMeekin method.[37] The results are reported in table 5. No change in the amount of nonprotein nitrogen, ascorbic acid or glutathione was found. The slight increases of glutathione and ascorbic acid following injection of sodium chloride are not statistically significant. The potassium content, however, rose from 340 to 386 mg., an increase of 13 per cent. The removal of water from the lens by the hypertonic ocular fluids would cause a slight increase of the contained constituents, but this could account for no more than 2 to 3 per cent of the rise.

TABLE 4.—*Penetration of Sodium Chloride into the Body Tissues*

	Na^+				Cl^-			
	Mg. per 100 Gm. Tissue †		mEq. per 100 Gm. Tissue †		Mg. per 100 Gm. Tissue †		mEq. per 100 Gm. Tissue †	
Tissue	Normal *	After Injection	Normal *	After Injection	Normal *	After Injection	Normal *	After Injection
Lung	250	443.2 ± 37.6	10.90	19.18 ± 1.65	260	365.1 ± 43.1	7.3	10.29 ± 1.22
Muscle	72	229.9 ± 16.9	3.1	10.00 ± 0.73	66	266.9 ± 16.5	1.8	7.52 ± 0.46
Heart	185	383.3 ± 56.9	8.0	16.66 ± 2.47	135	376.1 ± 36.4	3.8	10.62 ± 1.02
Spleen	...	243.6 ± 11.0	...	10.59 ± 0.48	160	285.5 ± 15.1	4.5	8.05 ± 0.50
Kidney	175	477.3 ± 12.4	7.2	20.70 ± 0.51	220	542.8 ± 15.1	6.2	15.31 ± 0.43
Liver	190	447.5 ± 18.2	8.2	19.47 ± 0.79	160	554.2 ± 18.2	4.5	15.65 ± 0.80

* Shohl,[23] p. 20.
† Calculated on a fat-free basis.

TABLE 5.—*Chemical Changes of Lens Produced by Intravenous Injection of Ten Per Cent Sodium Chloride*

Time	Ascorbic Acid, Mg. per 100 Gm. of Moist Lens	Glutathione, Mg. per 100 Gm. of Moist Lens	Nonprotein Nitrogen, Mg. per 100 Gm. of Moist Lens	Potassium, Mg. per 100 Gm. of Moist Lens
Before	4.23	268.2	156.1	340.2
After	4.41	274.5	156.1	385.9

COMMENT

The number and the chemical individuality of the compounds successfully employed in producing cataract suggest strongly that the active mechanism is a nonspecific one. We believe this mechanism to be on an osmotic basis. Furthermore, it is likely that cataracts produced by a variety of methods may be due fundamentally to an osmotic derangement, either local or systemic. Although this hypothesis has received but meager support in recent years, it seems to us to provide a rational

37. Koch, F. C., and McMeekin, T. L.: A New Direct Nesslerization Micro-Kjeldahl Method and a Modification of the Nessler-Folin Reagent for Ammonia, J. Am. Chem. Soc. **46**:2066-2069, 1924.

explanation for the onset of a large number of apparently unrelated clinical and experimental cataracts.

Changes in osmotic equilibrium between the aqueous humor and the lens may become manifest in a variety of ways, each of which under the proper conditions may become the immediate, predisposing cause of cataract. Among the manifestations of an osmotic upset might be listed (1) changes in the water content of the lens; (2) an alteration in permeability of the capsule; (3) an ionic imbalance resulting in convulsions, and (4) a sensitizing action on the lens proteins. Each of these changes has been suggested as playing a prominent role in production of opacities of the lens,[38] whereas any of them may quite easily be merely secondary to more fundamental osmotic changes. It must be remembered that alterations in a system as complex as that of the living cell are rarely uncomplicated. Similarly, changes in the lens may be due in part to any of a large number of factors comprehensively discussed in reviews on cataract.[39] However, we believe that in many cases the fundamental disturbance will be found to be osmotic.

The production of opacities in the lens might be visualized as follows: In the normal lens the individual cells are in contact and are separated from one another only by an intercellular cement substance (mucoprotein). Hypertonic solutions of various substances injected intravenously increase markedly the osmotic pressure of the blood and eventually that of the aqueous humor. The heightened osmotic pressure in the aqueous humor would tend to remove water from the lens fibers. A shrinking of the cells and a pulling away from one another would then result. Fluid would fill the intercellular spaces, and so-called water fissures would result. At this stage the lens might take on a cloudy appearance due to the destruction of optical contact of the cells and the differences of the refractive indexes of the intracellular and intercellular fluids. Cloudiness produced by such a mechanism would be analogous to mist made visible by the difference in refractive indexes of water and air.

Another factor operative in diminishing the transparency of the lens would be the destruction of the regularity of the lens fibers. Thus, the individual lens fibers might be transparent, but owing to their disorderly

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38. (*a*) Friedenwald, J. S.: Permeability of the Lens Capsule with Special Reference to the Etiology of Senile Cataract, Arch. Ophth. **3**:182-193 (Feb.) 1930; The Permeability of the Lens Capsule to Water, Dextrose and Other Sugars, ibid. **4**:350-360 (Sept.) 1930. (*b*) Schanz, F.: Die Wirkungen des Lichtes auf die lebende Substanz, Arch. f. d. ges. Physiol. **161**:384-396, 1915. (*c*) Bourne, M. C.: Metabolic Factors in Cataract Production, Physiol. Rev. **17**:1-27, 1937. (*d*) Kunde.[2] (*e*) Deutschmann.[3] (*f*) Löwenstein and Haurowitz.[9] (*g*) Köhnhorn.[12]

39. Duke-Elder, W. S.: Recent Advances in Ophthalmology, Philadelphia, P. Blakiston's Son & Co., 1934. Bourne.[38c]

arrangement the light rays would no longer be transmitted unimpeded but would be dispersed, giving a ground glass effect. This is comparable to the appearance of a diffusely scratched glass, which loses its transparency and becomes opaque. If the lens were examined histologically at this stage, no changes would be evident. Clinically, a scarred cornea in which the regularity of the stroma fibers is disturbed presents a similar picture. If injection is halted at this stage, the water may be reabsorbed, optical contact of the cells may be restored and regression of the opacity may result. However, if abnormal osmotic relations continue a variety of chemical changes may be visualized. The continued extraction of water from the lens fibers would concentrate the colloid and crystalloid constituents remaining in the cell. Eventually this might interfere with the normal interchange of nutrients and waste products; changes in p_H or other vital alterations would result, and death of the lens would supervene.

Such a picture is admittedly largely speculative. Nevertheless, the changes occurring during production of cataract are in harmony with this hypothesis. The histologic and slit lamp observations, for example, confirm the appearance of extracellular water producing water fissures. The rapid regression of experimental cataractous changes in the early stages points to a physical alteration, which is reversible, rather than to chemical, irreversible changes.

In a diabetic person, the abnormal concentration of dextrose in the blood and aqueous humor simulates the condition obtained by the injection of hypertonic solutions. Cataracts are not uncommon in young diabetic persons with the severe form of the disease. In the hyperglycemic stages the lens loses water and the eye becomes myopic.[40] In more advanced stages droplets of fluid are deposited underneath the capsule and opacities develop. Although we believe the water exchange to be the most important alteration, other contributing factors, also due to the abnormal concentration of dextrose in the eye, may enter into the picture. Dextrose and acetone have been shown to make the lens protein more sensitive to precipitation.[38b] High concentrations of dextrose have also been shown to decrease the permeability of the lens capsule.[41] Such a decrease would accentuate the osmotic differences across the membrane and might interfere with metabolism by decreasing the elimination of waste products or the availability of essential nutrients.

The cataracts produced by feeding galactose and xylose seem entirely analogous to the diabetic type, with one important exception. These

40. Granström, K. O.: Refraktionsveränderung bei Diabetes mellitus, Acta ophth. **3**:1-160, 1933.

41. Bellows, J., and Rosner, L.: Biochemistry of the Lens: XI. Effect of Galactose on the Permeability of the Capsule of the Lens, Arch. Ophth. **20**:80-84 (July) 1938.

sugars are not utilized by the body as readily as is dextrose. Therefore, hyperglycemia results more easily than with dextrose.[42] The increased sugar content of the blood produces a similar condition in the aqueous humor, and the sequence of events described for dextrose takes place, resulting in an alteration of the lens itself. Sasaki[43] has shown that galactose may appear in the aqueous in relatively high concentrations.

Darby and Day[44] suggested that the chemical similarity of xylose and galactose may somehow account for their cataractogenic properties. Such an assumption seems unnecessary. It is probable that any sugar not readily utilized by the body and reaching a high concentration in the blood and aqueous humor would similarly produce cataract if administered in adequate quantities. In support of this contention is the observation that arabinose, the molecule of which is geometrically distinct from those of galactose and xylose, also produced cataract when injected intravenously in hypertonic solution. The effects of galactose on the capsular permeability might increase its effectiveness as a cataractogenic agent. Whether xylose and arabinose similarly alter the lens capsule has never been investigated.

Patients with cholera frequently have cataract. Cholera is characterized by violent and prolonged diarrhea producing profound dehydration. A marked osmotic and fluid disturbance of the lens would seem unavoidable under such conditions. Dehydration through water deprivation alone with a resulting cataract has been reported.[45]

Senile cataract is usually more complex than any of the other types considered, since a number of factors are operating simultaneously. It seems reasonable to suppose, however, that with this form, too, osmotic disturbances may be fundamental. The decrease in renal and hepatic efficiency accompanying age is well known. Hyperglycemia is common.[46] Nitrogenous waste products are improperly eliminated, and their concentration in the blood rises. Accumulation of such compounds in the blood theoretically should act in a manner similar to intravenous injection of hypertonic solutions. Although the effect produced would

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42. Day, P. L.: Blood Sugar in Rats Rendered Cataractous by Dietary Procedures, J. Nutrition **12**:395-404, 1936.

43. Sasaki, T.: Untersuchungen der Linse, des Blutes und der Kammerwassers von Ratten bei Galactoseverfütterung: II. Ueber die Linsenkapselpermeabilität und über den Zuckergehalt von Blut, Kammerwasser und Linse bei der Galaktose Katarakt, Arch. f. Ophth. **138**:365-379, 1938.

44. Darby, W. J., and Day, P. L.: Xylose as a Cataractogenic Agent, Proc. Soc. Exper. Biol. & Med. **41**:407-408, 1939.

45. Kudo, T.: Studies on the Effects of Thirst: I. Effects of Thirst on the Weights of the Various Organs and Systems of Adult, Am. J. Anat. **28**:399-430, 1921.

46. O'Brien, C. S.: Hyperglycemia in Persons with Advanced Senile Cataract, Arch. Ophth. **6**:806-809 (Nov.) 1931.

be far less marked than that obtained in an acute experiment, its persistent action over long periods might produce the same result.

At present there is insufficient evidence to place the remaining types of cataract in the category of salt changes and osmotic upsets. It is not inconceivable, however, that later work will lead to their inclusion. For example, it seems possible that naphthalene, thallium and other poisons producing cataracts also cause damage to the liver. Since hepatic damage may cause disturbances of the water balance, cataract may easily arise from the consequent deranged water metabolism of the lens. Furthermore, naphthalene is known to produce hyperglycemia.[47] Cataracts formed by radiant energy are thought by Duke-Elder to be due fundamentally to increased capsular permeability. This in turn leads to a loss of glutathione and a change in the concentration of the salts and fluids of the lens sufficient to bring about opacities in a lens made more vulnerable by the short waves.[48] Until more data are available, however, there is little value in such purely speculative considerations.

Despite our consistent production of cataracts by hypertonic solutions, osmotherapy is not necessarily contraindicated by this consideration. The formation of opacities in dogs required about twenty times as much sodium chloride as is used clinically, calculated on the basis of body weight. Furthermore, clinical administration is of much shorter duration. However, it is conceivable that frequent repeated injections of hypertonic solutions may produce changes in the lens. Fortunately, if such procedures are necessary, it is comforting to remember that the early changes undergo rapid regression on discontinuance of the injections.

Our essentially negative chemical findings are further suggestive of the fundamentally physical nature of the cataracts produced by us. Thus, no change could be detected in the lenticular content of glutathione, ascorbic acid, or nonprotein nitrogen with onset of cataract. The slight increase of potassium is curious and at present inexplicable. The slow penetration of sodium and chloride into the lens is a further indication of the resistance afforded by the lens capsule to the passage of electrolytes. The effect of various crystalloids on the permeability of the capsule is now being investigated.

SUMMARY

Cataracts were produced in dogs and rats by continuous intravenous injections of various crystalloids for periods varying from twenty minutes

47. Michael, D., and Vancea, P.: Sur la multiplicité des voies par lesquelles on peut produire des lésions oculaires naphthaliniques, Compt. rend. Soc. de biol. **96**:63-65, 1927.

48. Duke-Elder, W. S.: The Pathological Action of Light upon the Eye: II. Action upon the Lens, Theory of the Genesis of Cataract, Lancet **1**:1250-1254, 1926.

to seven hours. Solutions (approximately isotonic with a solution of 10 per cent sodium chloride) of sodium sulfate, lithium chloride, sodium chloride, galactose, arabinose, xylose, glycerin, ethylene glycol, amino-acetic acid, sodium lactate and ethyl alcohol were effective cataractogenic agents when administered in this manner.

Regressive changes were observed if the injections were discontinued after cataract was apparent and the animal allowed to recover.

A loss in weight of the whole eye followed the intravenous injection of 10 per cent sodium chloride. Among the individual tissues, the lens showed the greatest percentage loss of water, with the retina, cornea, sclera and vitreous following in that order.

After injection of sodium chloride each of the ocular tissues showed a marked rise in sodium and chloride, with the exception of the lens, which remained almost unchanged. Of the organs and skeletal tissues, the muscle showed the greatest rise, followed by the kidney, liver, heart, lung and spleen in that order.

The osmotic pressure (as measured by the freezing point depression) of the blood, aqueous humor and spinal fluid increased directly with the rise in sodium and chloride of these fluids.

The hemoglobin content of the blood decreased during injection, indicating hemodilution.

The ascorbic acid, glutathione and nonprotein nitrogen concentrations of the cataractous lens did not differ from those of the normal lens.

The potassium content of the cataractous lens was 386 mg. per hundred grams as compared with 340 mg. in the normal lens.

The possible significance of these findings in the pathogenesis of cataract is discussed.

Profs. S. R. Gifford and C. J. Farmer made many valuable suggestions concerning this study.

SIZE AND LOCATION OF THE BLINDSPOT OF MARIOTTE

AS COMPUTED FROM ONE HUNDRED ANGIOSCOTOMETRIC RECORDS

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BROOKLYN

In an attempt to determine whether or not the blindspot of Mariotte as represented on the standard campimeter chart is appropriate for studies with minute test objects, such as those used in angioscotometry, it was decided to analyze a series of 100 blindspots of "normal" subjects.

This seemed particularly necessary because of the great variation in the technics employed by previous workers [1] whose figures have been used as standards for the location and dimension of the blindspot on standard instruments, such as the tangent screen, the campimeter and the stereocampimeter.

The material studied was obtained by permission of Dr. John N. Evans [2] and was selected from the records of his private patients. Only those subjects were accepted who had undergone a careful general physical and ophthalmic review and who showed no evidence of nephritis, arteriosclerosis, sinal disease, myopia, tumor of the brain, optic neuritis, medullated nerve fibers, etc. In other words, every attempt was made to avoid abnormal changes and to create reproducible conditions.

Regarding the technic employed, the following paragraphs are quoted directly from Evans' "Clinical Scotometry":

1. Usual precautions for control of position, comfort, distractions, etc., are taken.

2. Distant correction should, as a rule, be worn.

From the Department of Ophthalmology, the Long Island College of Medicine.

1. Gradle, H. S.: The Blind Spot, Illinois M. J. **28**:170 (Jan.) 1915; The Blind Spot: First Communication, Ann. Ophth. **24**:637 (Oct.) 1915; The Blind Spot: Second Communication, ibid. **25**:740 (Oct.) 1916; The Blind Spot: III. The Relation of the Blind Spot to Medullated Nerve Fibers in the Retina, J. A. M. A. **77**:1483 (Nov. 5) 1921. Gradle, H. S., and Meyer, S. J.: The Blind Spot, Am. J. Ophth. **12**:802 (Oct.) 1929. Haycroft, J. B.: Method of Mapping Blind Spot of Retina, Lancet **2**:518, 1911. Peter, L. C.: Perimetric Studies of the Normal and Pathological Blind Spot of Mariotte, Ann. Ophth. **25**:261 (April) 1916. Van der Hoeve, J.: The Size of the Blind Spot and Its Distance from Point of Fixation in the Emmetropic Eye, Arch. Ophth. **41**:350, 1912.

2. Evans, J. N.: Clinical Scotometry, New Haven, Conn., Yale University Press, 1938, pp. 61-64.

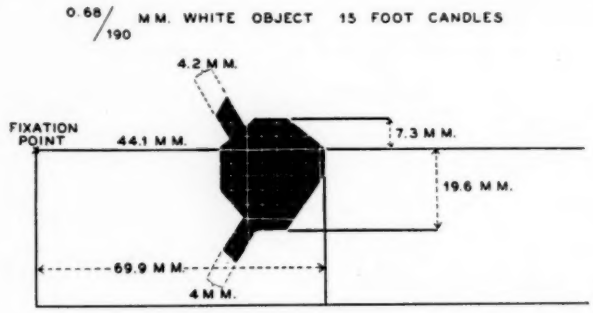
3. The stereocampimeter and Lloyd chart are advocated. If both eyes are used (binocular fixation), the muscle balance should be checked and corrected by the instrument.

4. The lamp used is one especially designed to give shadowless illumination, standardizable and uniform in color and quality, supplying an intensity of fifteen foot candles measured on the slate with the General Electric Company's foot candle meter. It is so attached that the light maintains the same relation to the slate during adjustments of the instrument, and is passed through ground glass to give the quality of daylight.

5. The method of signaling is usually by tapping.

6. Markings are made with a light-colored, fine-pointed wax pencil (of the newer metal-magazine type) directly, instead of being copied from the slate on white records. As suggested by the writer, this method reduces time and effort about fifty per cent.

7. The subject is allowed to close his eyes frequently, but must not change his position.



Average measurement of 100 normal blindspots.

8. The blind spot is outlined as usual by passing from the seeing to the non-seeing area, and a line connecting the dots is then drawn.

9. The object is next moved around the periphery of the blind spot, a millimeter from it, until it suddenly disappears, when a dot is marked. This place is then approached from the opposite direction and at right angles to the supposed course of the vessel, but at about 2 mm. farther from the edge of the blind spot and its point of disappearance noted again. Alternate sides are thus plotted, each point being about 1 mm. in advance of the preceding. In this way branching and cross vessels are not missed, and the twistings and widenings are easily followed. As the object is approaching the vessel, it may be given very fine movements parallel to the vessel.

10. If a crossing is picked up far out, it can be traced in a similar way to the nerve head, but it is more difficult to locate a vessel far out in the field without having led to it while mapping.

11. The patient may rest as often as necessary; but each time work is resumed, one or two points of the map should be checked until the new plot coincides.

One hundred blindspots thus mapped were measured, and the results (in millimeters) were charted and averaged (see accompanying chart and table).

(The objects used were white spheres mounted on black wire stems. The slate on which the mapping was done was dull black with a gray imprint in the pattern suggested by Lloyd. The fixation distance of the instrument was 90 mm. A columnating lens was positioned before the eye. Monocular fixation was used. The eye not being tested was covered by an appropriate occluder which did not exert pressure on the eyeball.)

CONCLUSIONS

Measurements of 100 normal blindspots were made to determine whether the blindspot as usually represented on the campimeter slate is a satisfactory standard to use when one is applying the technic advocated for angioscotometry. The general variation in the figures obtained

Data on Measurements of One Hundred Blindspots (Angioscotomeric Technic)

Region Measured	Total Number of Measurements	Total in Mm.	Average in Mm.	Transposition to		
				Minutes	Seconds	Degrees
Macula to nasal border	101	4,458.1	44.1	4	2	13
Width of blindspot	103	2,397.9	25.8	44	0	7
Macula to temporal border	96	6,722.5	69.9	11	53	20
Area scotoma units	101	1,217.5	12.0			
Above horizontal	108	794	7.3	12	..	2
Below horizontal	103	2,021.5	19.6	53	20	5
Vessel stump 1 degree from border of blindspot						
Above	94	400.7	4.2	16	..	1
Below	74	300.9	4.0	12	20	1
Object size	99	67.79	0.68			

in this study from those given by previous workers using different technics indicates a larger blindspot. This is obviously due to a number of causes besides variation of light, such as size of the test object and contrast with the background. One must, however, appreciate that the angular size of the object is not purely a mathematical relation and that because of the method employed mapping of the blindspot was impossible between the retinal vessels. In support of this contention the reader is referred to the evidence of numerous workers as reviewed by Duke-Elder.[3] Immediately adjacent to the zone of absolute blindness at the blindspot is a narrow zone in which the 2/2,000 isopter may not be plotted. This is said to be due to the reduced number of rods and cones in the peripapillary area but may be due to the defect arising from the effect of the vascular circle of Zinn and its associated perivascular mechanism.

3. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1932, vol. 1, p. 896.

RETROBULBAR INJECTIONS OF ATROPINE SULFATE FOR ATROPHY OF THE OPTIC NERVE

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AND
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Many different treatments have been used in an attempt to improve the loss of vision due to atrophy of the optic nerve. Up to the present time little hope for improvement has been given. After a review of the literature two years ago, it was decided to try at the University of Arkansas School of Medicine the treatment described by Fejér,[1] Kosmin,[2] Lauber[3] and Cordes.[4] This treatment consists of retrobulbar injections of a solution of atropine. The only rational reason that improvement could be expected from this treatment in cases of atrophy of the optic nerve would seem to be that it increases the arterial circulation to this nerve. Several different types of atrophy were treated by this method. The outline of treatment given by Kosmin[2] was used. This consisted of the injection of a 0.1 per cent aqueous solution of atropine sulfate into the retrobulbar space twice weekly in increasing doses. A series of graduated doses (0.3 cc., 0.5 cc., 0.7 cc. and a maximum of 1 cc.) was given to a total of ten injections. This series will be referred to later in this paper as a course of injections. The injections were placed as nearly as possible in the retrobulbar space, 6 mm. behind the globe, near the optic nerve.

Only 5 patients returned for sufficient treatment and examination to make the data worth while in evaluating the results. In 1 of these the condition accompanied arteriosclerosis; in 1 it accompanied retrobulbar neuritis; in 1 it followed syphilitic optic neuritis, and in 2 it was associated with syphilis of the central nervous system.

1. Fejér, J.: Ueber den Wert der Atropinbehandlung insbesondere der tabischen Opticusatrophie, Arch. f. Augenh. **110**:76-89, 1936.

2. Kosmin, V. I.: Retrobulbar Injection of Atropine in Therapy of Atrophy, Sovet. vestnik oftal. **9**:686-692, 1936.

3. Lauber, H. J.: Treatment of Atrophy of Optic Nerve, Arch. Ophth. **16**:555-568 (Oct.) 1936.

4. Cordes, F. C.: Retrobulbar Injection of Atropine in Arteriosclerotic Atrophy, Am. J. Ophth. **20**:53-55 (Jan.) 1937.

REPORT OF CASES

CASE 1.—E. R. B., a Negress aged 78, came to the clinic on April 27, 1937, complaining of gradual loss of vision for twenty years.

Diagnosis.—A diagnosis of arteriosclerosis, bilateral atrophy of the optic nerve and aphakia of the right eye was made.

History.—The patient stated that she had had an operation for cataract in the right eye twenty years previously, with no improvement. The visual acuity in the left eye had been gradually failing.

Examination of Eyes.—Right Eye: There was a scar in the superior portion of the cornea. The lens had been extracted at the time of iridectomy. The vitreous was clear. The optic disk was very pale. Vision was limited to light perception. Left Eye: The cornea and media were clear; the optic disk was white; the retina was atrophic, and the blood vessels were small and tortuous. The patient could count fingers at 4 feet (120 cm.). The vision being so poor, charts of the visual fields could not be made.

General Examination.—Generalized arteriosclerosis was present. The blood pressure was 176 systolic and 96 diastolic. The urine was alkaline and had a specific gravity of 1.016; it contained no albumin or sugar. The Wassermann and Kline reactions were negative.

Course and Treatment.—The patient was given saturated solution of potassium iodide, 5 drops three times per day for three months, with no change in the visual acuity. Retrobulbar injections of a 0.1 per cent atropine sulfate solution were started. She was given three courses of treatment in each eye. After the first course she reported some improvement in vision, which, however, could not be confirmed on examination. After the final injection, the vision in the right eye was limited to light perception and in the left eye was 20/200.

Follow-Up Examination.—She was reexamined on Jan. 10, 1940, three months after the last injection. Little change was seen in the eyegrounds, and the vision was the same as at the previous examination. She stated that she was able to see her way about and was pleased with the improvement.

CASE 2.—R. L. R., a white man aged 30, came for examination on Sept. 27, 1937, complaining of loss of vision for six months.

Diagnosis.—The diagnosis was atrophy of the optic nerve following retrobulbar neuritis.

History.—The patient stated that he had had a severe injury to the head six months previously, gradually followed by loss of vision. No details of the injury were available, and no roentgenograms had been taken. He stated that he had used alcohol and tobacco to excess for years.

Examination of Eyes.—Both eyes were normal except for very pale nerve heads. The retinal blood vessels were slightly decreased in size. Vision was 2/200 in each eye. There was no color perception. The visual fields are shown in chart 1 *A*.

Physical Examination.—Physical examination revealed no apparent pathologic change. Roentgen examination of the teeth showed no periapical abscesses. The Wassermann and Kline reactions were negative.

Course and Treatment—The patient was given saturated solution of potassium iodide for one year, with no improvement in visual acuity. Starting on Sept. 3,

1938, he was given three complete courses of retrobulbar injections of atropine sulfate solution in each eye. He reported immediate improvement following the first three injections, up to 6/200 in each eye. The vision after the final treatment was 8/200 in each eye. He reported that he could distinguish blue and red. There was little change in his visual fields (chart 1 *B*).

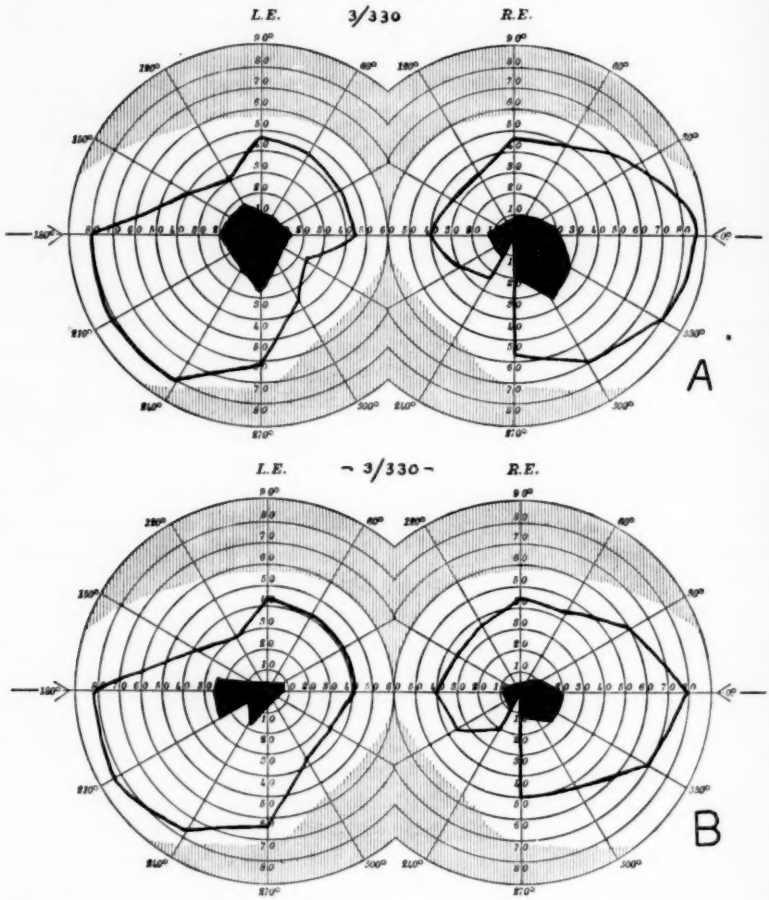

Chart 1 (case 2).—Visual fields of R. L. R. on Sept. 27, 1937 (*A*) and on Feb. 23, 1940 (*B*). Visual acuity on the earlier examination was 2/200; on the later examination it was 8/200.

CASE 3.—Z. H., a white woman aged 23, came for examination on Nov. 28, 1938, complaining of loss of vision for two weeks.

Diagnosis.—The diagnosis was syphilitic optic neuritis followed by atrophy.

History.—She had noticed an impairment of vision three weeks previously, which rapidly became worse. At no time prior to this had she ever had any trouble with her eyes. She stated that she had had a small nodule on the vulva which lasted about two weeks.

Examination of Eyes.—Right Eye: The cornea and the lens were clear. There were a few floating opacities in the vitreous. The retina and the optic nerve head appeared swollen. Vision was limited to light perception. Left Eye: The description of the right eye applies also to the left. The vision was 5/400.

Physical Examination.—Physical examination revealed no evidence of pathologic change. The Wassermann and Kline reactions were 4 plus. Roentgen examination of the teeth revealed no abnormality.

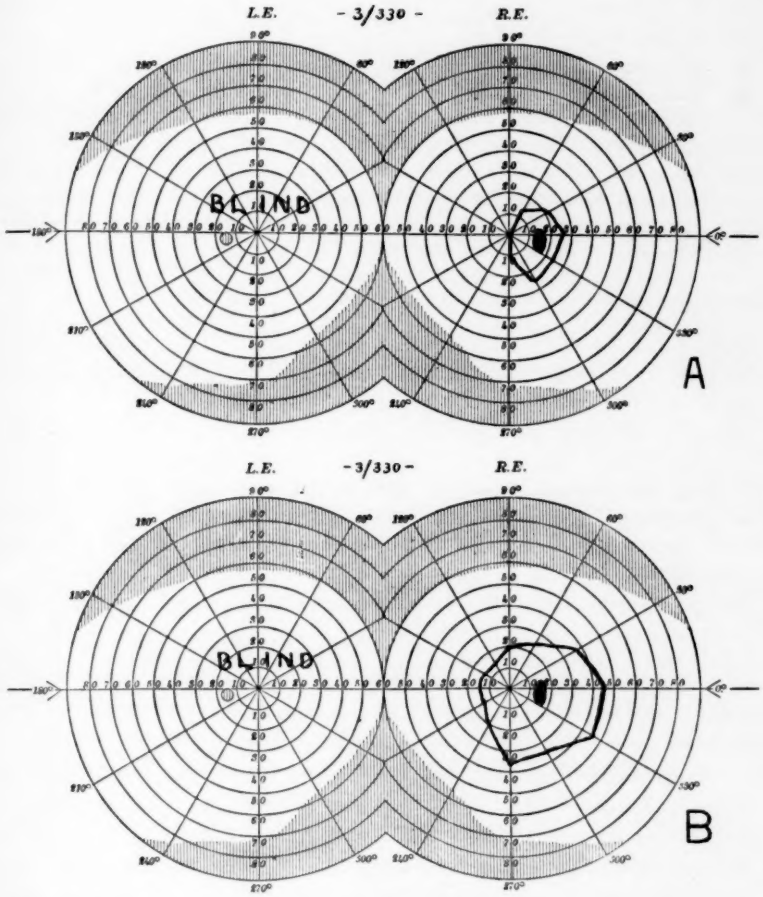

Chart 2 (case 3).—Visual fields of Z. H. on April 2, 1939 (*A*) and on June 18, 1940 (*B*). Visual acuity on the earlier examination was 20/100; on the later examination it was 20/40-2.

Treatment and Course.—The patient was given saturated solution of potassium iodide, 10 drops three times per day, with an increase of 1 drop per dose per day until 30 drops per dose per day was reached. On December 2 weekly intramuscular injections of 1 cc. of mercury salicylate were started. Examination on Jan. 25, 1939, showed that the swelling of the optic nerve head had disappeared. The central retinal vessels were much smaller in diameter than normal. The optic

nerve head was slightly pale. At this stage retrobulbar injections of atropine sulfate solution were started. For the purpose of evaluating this treatment, only her worse eye was used. The vision in the right eye at this time was limited to light perception. The vision in the left eye was 5/200. The visual fields could not be taken. She received two courses of treatment in the right eye before injections were started in the left eye. After these two courses the visual acuity in the right eye was 20/100. The visual fields at this time are shown in chart 2 *A*. The vision in the left eye was 2/400. She was then given another course in the right eye. Administration of the iodides and mercury salicylate was continued during this period.

She was reexamined on June 30. The right eye showed the cornea and the lens normal. The vitreous was clear, and the optic nerve head was normal in color. The superior temporal artery was obscured by a large area of chorioretinitis, which was apparently inactive. The remaining three retinal arteries appeared normal. The central visual acuity, with proper refraction, was 20/70. The left eye showed the vitreous filled with opacities similar to those observed in the first examination. Posterior synechiae were present. The outline of the optic nerve head could not be clearly made out. The vision was 2/400. Examination on June 18, 1940, gave similar results. The improvement in the visual fields is shown in chart. The visual acuity was 20/40-2.

CASES 4 AND 5.—H. C., a white man aged 32, and R. C. J., a white farmer aged 48, came for examination in November 1938, complaining of almost complete loss of vision for over one year.

Diagnosis.—In each case the diagnosis was neurosyphilis and bilateral atrophy of the optic nerve.

Examination of Eyes.—The optic nerve heads were pale, with a decrease in the size of the retinal blood vessels. No other pathologic condition was noticed. Vision in the case of H. C. was limited to counting fingers at 1 foot (30 cm.). Vision in the case of R. C. J. was limited to light perception.

Physical Examination.—The Wassermann and Kline reactions of the blood and of the spinal fluid were 4 plus in each case.

Course and Treatment.—The patients had been given potassium iodide and a mercury compound intramuscularly before the eyes were examined. Each was given two complete courses in each eye of retrobulbar injections of atropine sulfate solution. No improvement of vision was noted in either case after this amount of treatment; so no further injections were given.

SUMMARY

It is apparent that in certain cases the increase in the blood supply to the optic nerve produced by retrobulbar injections of atropine sulfate does improve vision to some degree in cases of atrophy of the optic nerve.

In 2 cases of syphilis of the central nervous system of long standing no improvement in visual acuity was noticed after twenty injections in each eye.

Treatment of atrophy of the optic nerve by retrobulbar injections of atropine sulfate solution was especially effective in a case of early atrophy following syphilitic optic neuritis.

The improvement in vision gained by this treatment has remained stationary in 3 cases.

TREATMENT OF RETINITIS PIGMENTOSA WITH RETROBULBAR INJECTIONS OF ATROPINE SULFATE

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For almost a century ophthalmologists have had under consideration the vascular system in relation to retinitis pigmentosa. For many years the condition was believed to be mainly local. More recently a consideration of glandular disturbance, cerebral abnormalities, cerebral malfunction, deafness and congenital disfigurations crept into the picture, and it has been considered that retinitis pigmentosa is only part of a general disease picture.

From the standpoint of therapy the interest still centers on the vascular picture in the eye, and practically all treatment has been designed to improve, directly or indirectly, the circulation in the choriocapillaris.

The use of atropine sulfate retrobulbarly is not new. Abadie [1] employed the drug in 1923 in the treatment of atrophy of the optic nerve and reported a good result.

Samkowski [2] treated syphilitic atrophy in a number of cases with retrobulbar injections, hoping to achieve a local orbital hyperemia. He thought that his patients were improved.

In 1931 Mariotti and Lugli [3] reported improvement in 6 of 11 cases of atrophy.

In 1937 Cordes [4] reported a case of atrophy of the optic nerve which was improved after retrobulbar injection of atropine sulfate.

Folk [5] reported a series of cases of atrophy treated with paracenteses and with atropine sulfate injected retrobulbarly. In this group there were 2 cases of retinitis pigmentosa in which improvement was obtained.

Although I do not feel that true atrophy occurs in association with retinitis pigmentosa until a very late stage, when the glial deposits have killed the third neuron, the principle of vasodilation is just as important

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The research for this paper was done while the author was a resident surgeon in the Division of Ophthalmology at the Henry Ford Hospital, Detroit.

1. Abadie, C.: Ann. d'ocul. **160**:385, 1923.
2. Samkowski, J.: Arch. oftal. **3**:286, 1927; cited by Folk.[5]
3. Mariotti and Lugli: Paper read at the meeting of the Società oftalmologica italiana, October 1931; cited by Folk.[5]
4. Cordes, F. C.: Am. J. Ophth. **20**:53 (Jan.) 1937.
5. Folk, M. L.: Am. J. Ophth. **20**:511 (May) 1937.

or more so, because the equatorial genesis of retinitis pigmentosa occurs in the region of the eye's poorest vascularity.

This paper reports the results in 6 cases in which the patients were treated with retrobulbar injections of atropine sulfate and were available for an average two year check.

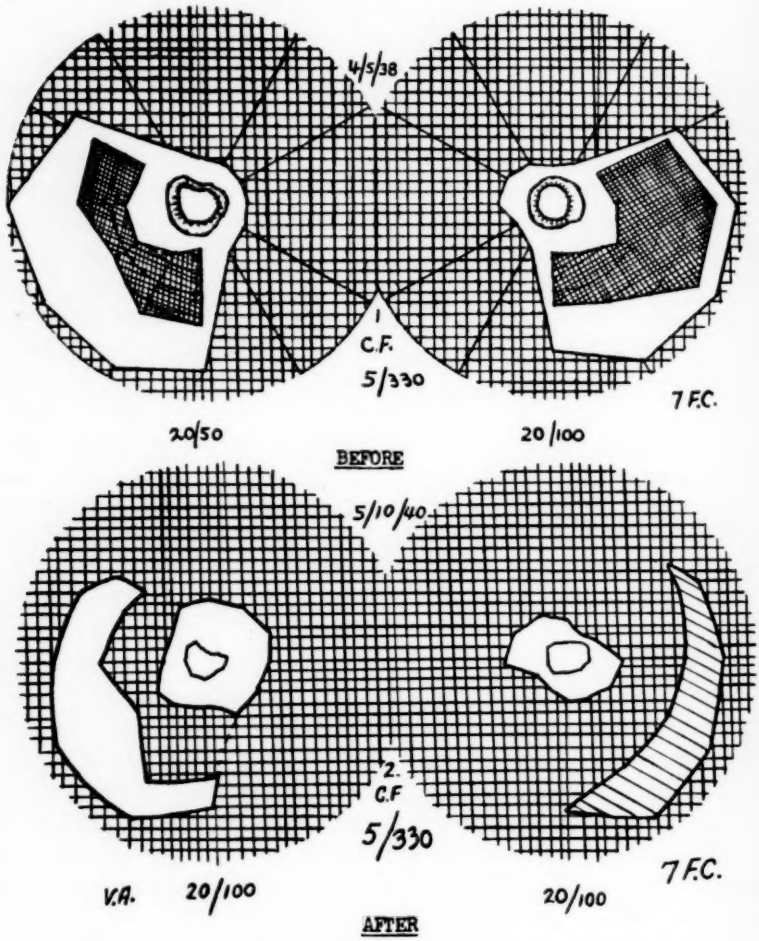

Chart 1.—Visual fields in case 1

The patients were all in the third and fourth decades of life. None had any syphilitic stigma. None had any evidence of glandular disturbance, congenital structural abnormalities or deafness. All had normal cholesterol and icteric index levels, and the van den Bergh reactions were normal. This statement does not mean that some were excluded

from the study because of abnormality but rather that no abnormalities were present. They were all well nourished persons whose only complaint was blindness, and aside from the generalized vascular dysfunction previously reported nothing abnormal was noted on general examination.

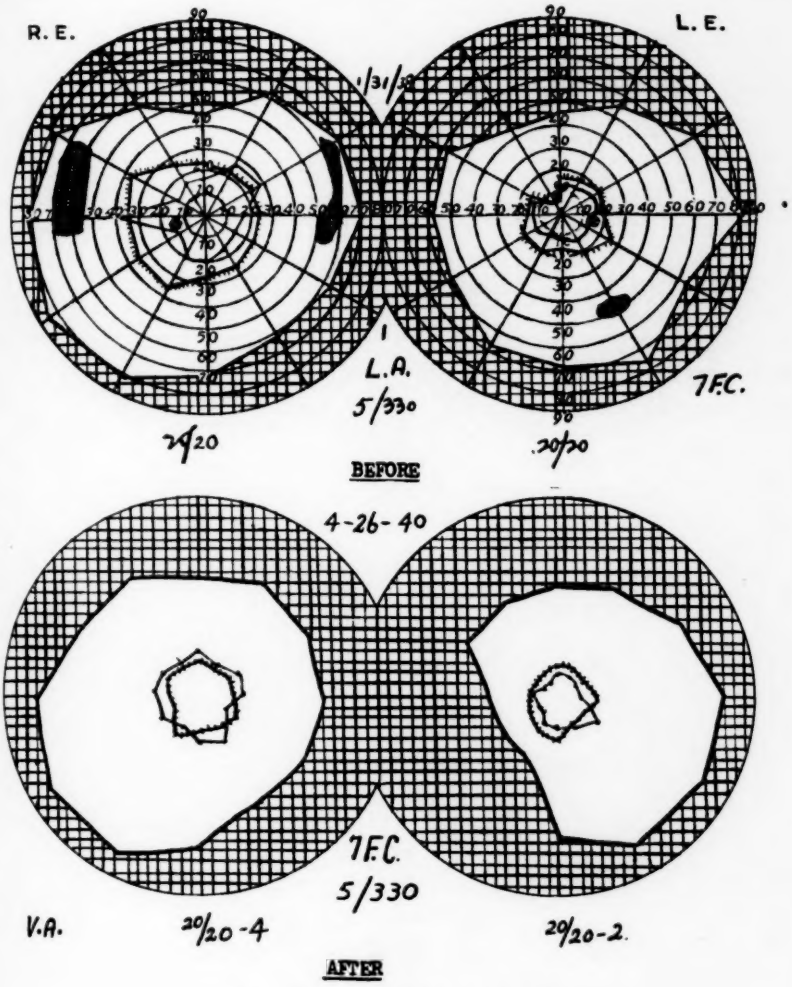

Chart 2.—Visual fields in case 2.

The patients presented the classic picture of retinitis pigmentosa as regards marked narrowing of arteries in the retina, bone corpuscle pigment deposits at the equator and waxy disks. In 1 or 2 cases the condition was advanced enough to show pigmentation extending into the macular area.

Retrobulbar injection of 1 cc. of 1 : 1,000 atropine sulfate solution was made into the muscular cone twice weekly, alternating eyes. A long 24 gage needle and a Luer Lok syringe with a ring plunger were used. The solution was sterilized in a small Erlenmeyer flask, 2 or 3 cc. to the flask, and after the required amount was aspirated the remainder was

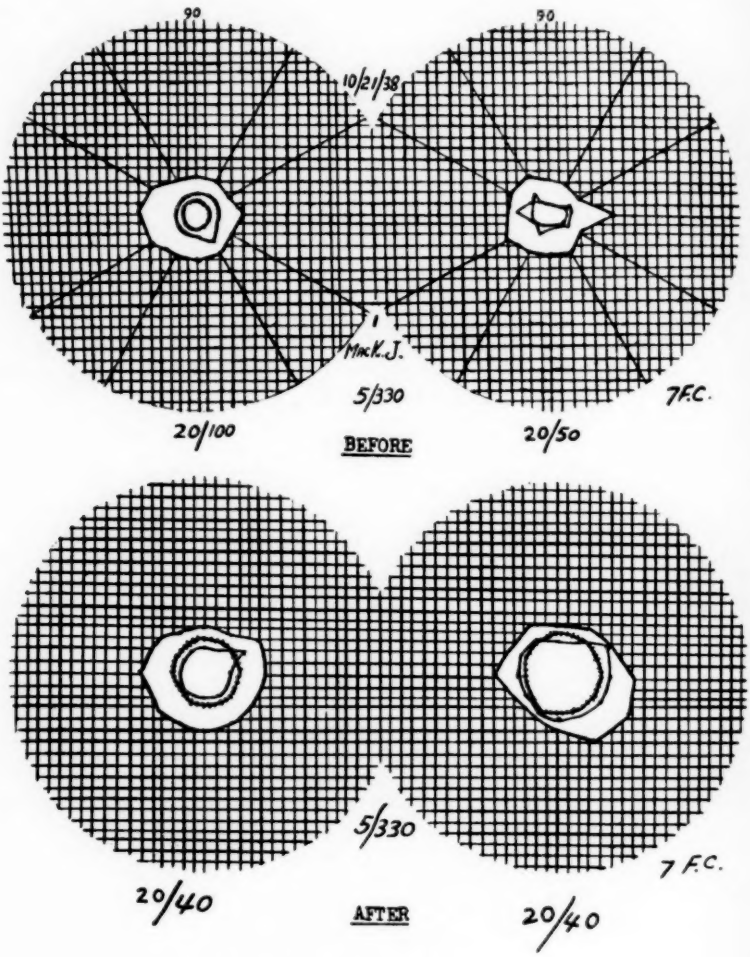

Chart 3.—Visual fields in case 3.

discarded. Needless to say, every precaution was taken to insure the solution being sterile when it was deposited in the muscle cone. As a result, there were no infections.

The injections are not painful unless the periosteum is touched with the needle point. The manner of injection is the same as that commonly used for reaching the ciliary ganglion.

REPORT OF CASES

CASE 1.—When first seen, the patient had corrected vision of 20/50 in the right eye and 20/100 in the left. He received twenty injections in each eye during the next five months. At the end of this treatment vision in the right eye had improved to 20/40; that in the left eye remained at 20/100. After two years and

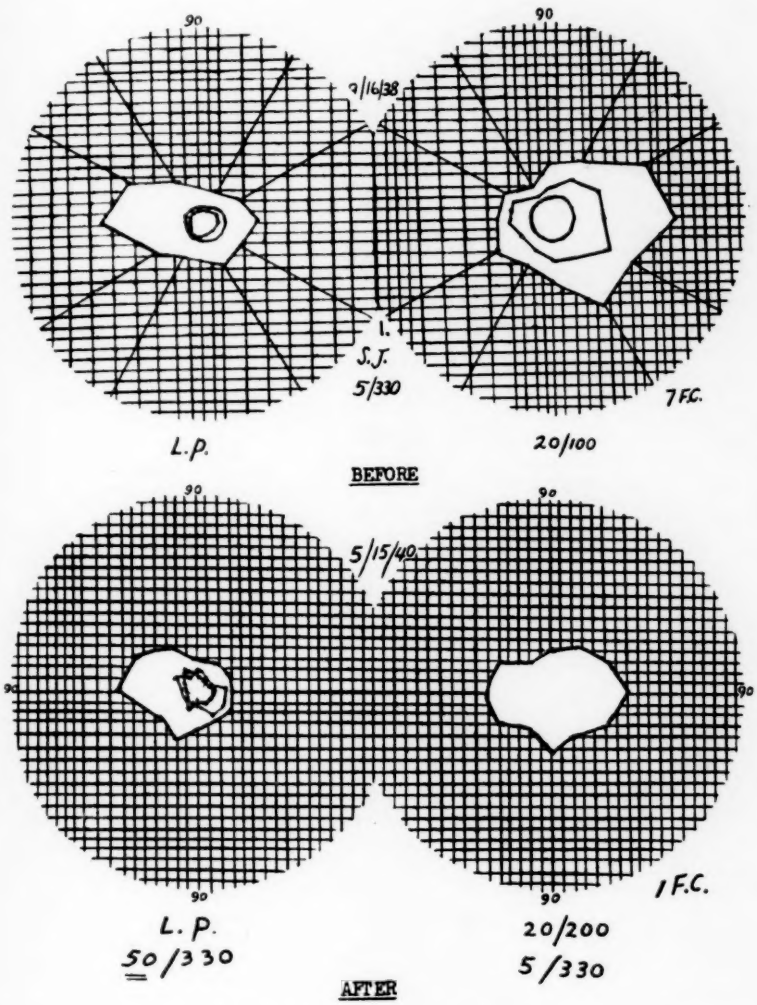

Chart 4.—Visual fields in case 4.

four months the corrected vision is 20/100 in each eye. The fields have constricted, and he now has only bare perception for red centrally.

CASE 2.—A young woman had only minimal involvement, her vision being 20/20 in each eye on her appearance at the clinic. There were some small oval scotomas

at the equator projection. Six injections of atropine sulfate were given in each orbit, and these scotomas disappeared. She came back after two years and they had not reappeared, her vision remaining at 20/20 in each eye. The fields showed some narrowing for form and color but not much. I feel that the condition in this case is probably arrested.

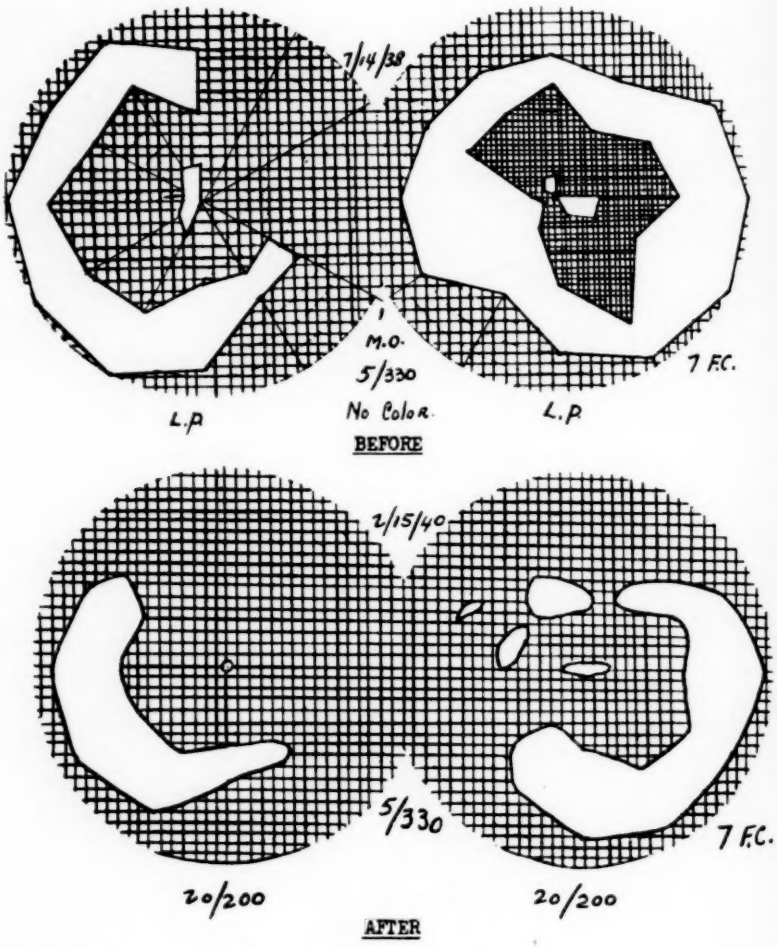

Chart 5.—Visual fields in case 5.

CASE 3.—When the patient was seen vision in the right eye was 20/100 and in the left 20/50. In addition to retinal changes she had a very small early cataract of the posterior cortical type. Fifteen injections in each eye were given, and vision improved to 20/40 in each eye. A year and a half later her vision was 20/40 in the right eye and 20/30 + 2 in the left, with considerable enlargement of the fields for form and color. At present the retina is about the same, and no advancement of the lens opacity is noted.

CASE 4.—Initial vision in this case was limited to light perception in the right eye and 20/100 in the left. Eight injections in each eye were given, without improvement. Far advanced cataracts were noted. Eventually the patient insisted on cataract extraction, and this was done, with, as was expected, no improvement. After two years she could barely see fingers at 1 foot (30 cm.) with the right eye, and the vision in the left eye was 20/200. Her visual fields showed steady

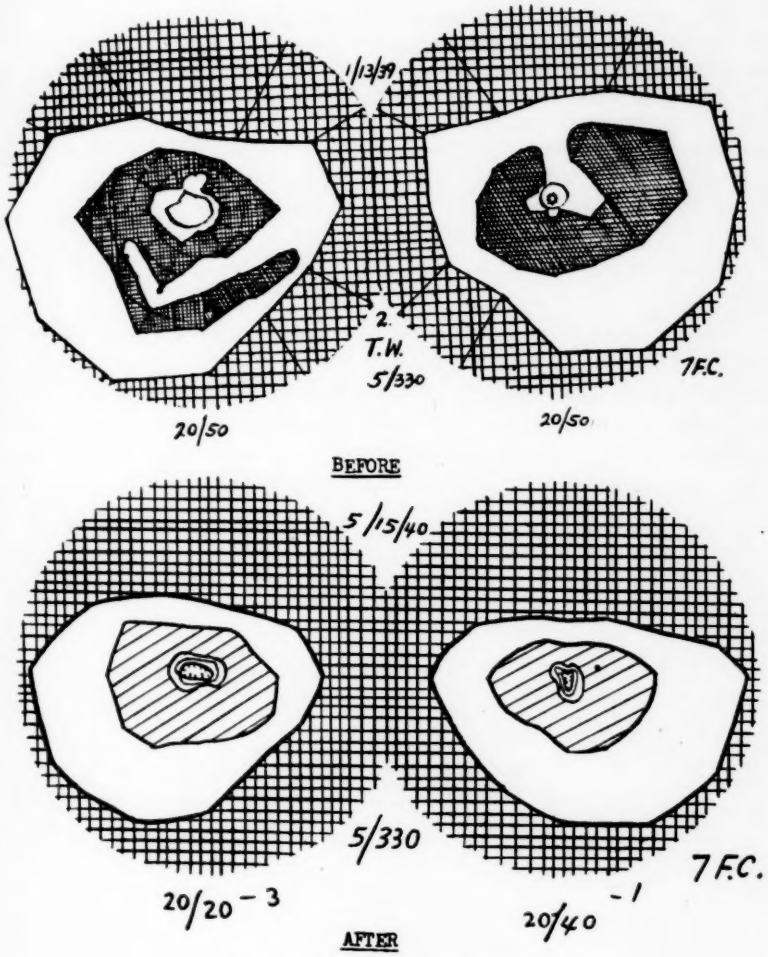

Chart 6.—Visual fields in case 6.

loss for form and color. The follow-up field of the right eye was taken with a 50 mm. object, while that of the left eye was taken as usual with a 5 mm. object at 330 mm. At present she can see a 17.5 mm. colored object with the left eye.

CASE 5.—Vision in this case was limited to light perception when treatment was begun. The patient had, in addition to retinal changes, an early cataract

formation in each lens. Twenty injections were made on each side, and her vision improved to 20/200 in each eye. She was overjoyed at the improvement. At the time of writing this has been maintained for almost two years, but her fields are definitely worse. It is highly questionable that there is real improvement with the fields steadily shrinking, but the central vision holds up well, and the patient now is able to work, which was impossible before.

CASE 6.—Vision in this case was 20/50 uncorrected when treatment was begun. The fields contained heavy ring scotomas in each eye, with color perception practically gone, the loss for blue being greater than that for red. During the next three months the patient had fifteen injections in each eye. Vision in the right eye improved to 20/30, and one letter in the 20/40 line was added to the left eye's vision. Four months later vision in the right eye had dropped back to 20/50. After five more injections vision in the right eye went back to 20/30, and after two years his vision was 20/30 — 3 in the right eye and 20/40 in the left. This man was benefited by treatment.

SUMMARY

Six patients with retinitis pigmentosa were treated with retrobulbar injections of 1 : 1,000 atropine sulfate and followed for two years.

Two showed definite improvement; the condition of 1 was apparently arrested, and 3 showed no improvement.

Retrobulbar injections of 1 : 1,000 atropine sulfate are apparently of benefit in some cases of retinitis pigmentosa; in this series the incidence of improvement was 50 per cent.

CORRELATION OF THE RESULTS OF THE BIO-PHOTOMETER TEST WITH THE VITAMIN A CONTENT OF HUMAN BLOOD

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During the last fifteen years the work of many investigators has established a relation between some phases of visual acuity and the state of vitamin A nutrition in animals (for full bibliography see the articles by McCollum and his associates [1] and Hecht [2]). Fridericia and Holm [3] showed that night blindness is an early symptom of vitamin A deficiency. Wald [4] demonstrated that vitamin A enters into the constitution of the visual purple, which constantly traverses a cycle of breakdown and resynthesis when light falls on the retina. In the absence of a fresh supply of vitamin A carried by the circulation the resynthesis is retarded and the visual threshold of the eye is raised; this is the change underlying the onset of some night blindness.

As a result of these findings it has seemed logical to explore the possibility that night blindness in man (when there is no local pathologic condition of the eye) is frequently due to subnormal vitamin A nutrition. A suitable technic for measuring quantitatively the visual threshold during adaptation to darkness has been sought, so that data may be collected on which to base a criterion of normality in dark adaptation. Departure from this criterion might then afford a measure of vitamin A

Engineering Experiment Station Project of the North Carolina State College, conducted by the cooperation of the State College Department of Chemistry and the Duke University Medical School.

1. McCollum, E. C.; Orent-Keiles, E., and Day, H. G.: The Newer Knowledge of Nutrition, New York, The Macmillan Company, 1939.

2. Hecht, S.: Rods, Cones, and the Chemical Basis of Vision, Physiol. Rev. **17**:239, 1937.

3. Fridericia, L. S., and Holm, E.: Experimental Contribution to the Study of the Relation Between Night Blindness and Malnutrition, Am. J. Physiol. **73**:63, 1925.

4. Wald, G.: Carotenoids and the Visual Cycle, J. Gen. Physiol. **19**:351, 1935.

undernutrition in subjects who displayed no other clinical signs of deficiency. A number of methods for making the necessary measurements have been proposed, several of which involve the use of specially designed instruments (Jeans and Zentmire;[5] Edmund and Clemmesen;[6] Jeans, Blanchard and Zentmire;[7] Feldman;[8] Hecht and Shlaer;[9] Pett;[10] Haig and Lewis[11]).

We record certain experiences with one of these instruments, the biophotometer introduced by Jeans and his associates.[7] Our aim was to examine a number of subjects by the standard biophotometer test of these authors and at the same time to measure the vitamin A and the carotene content of the plasma. The degree of correlation between the results of the two tests was then calculated.

EXPERIMENTAL DATA

The subjects of the observation were 71 healthy persons, chiefly college students subsisting on their ordinary diets. Nine were tested on two occasions, before and after treatment, with 25,000 U. S. P. units (international units) of vitamin A in shark liver oil daily for five days. Thus eighty pairs of readings were made for comparison of the biophotometer readings with the level of vitamin A in the blood.

Determination of the Level of Vitamin A in the Blood.—The method of May[12] was employed, with a slight variation. A sample of blood was obtained by venipuncture, oxalated and centrifuged. Two cubic centimeters of plasma was pipetted off and run into a 15 cc. test tube. Two cubic centimeters of 95 per cent alcohol was added to the plasma, and the tube was shaken; then 3 cc. of purified petroleum benzine (petroleum ether) (boiling range, 35 to 60 C.) was added, and the tube was stoppered and shaken vigorously for ten minutes. The tube was placed in the centrifuge and spun until the petroleum benzine layer was completely separated. It measured 3 cc. in all. One cubic centimeter was taken for reading the carotene in the photoelectric microcolorimeter of Evelyn and Cipriani,[13] the 440 millimicron filter being used and the optical density being

5. Jeans, P. C., and Zentmire, Z.: A Clinical Method for Determining Moderate Degrees of Vitamin A Deficiency, J. A. M. A. **102**:892 (March 24) 1934.

6. Edmund, C., and Clemmesen, S.: On Deficiency of A Vitamin and Visual Dysadaptation, London, Oxford University Press, 1935.

7. Jeans, P. C.; Blanchard, E., and Zentmire, Z.: Dark Adaptation and Vitamin A, J. A. M. A. **108**:451 (Feb. 6) 1937.

8. Feldman, J. B.: Dark Adaptation as a Clinical Test, Arch. Ophth. **15**:1004 (June) 1936.

9. Hecht, S., and Shlaer, S.: Adaptometer for Measuring Human Dark Adaptation, J. Optic. Soc. America **28**:269, 1938.

10. Pett, L. B.: Vitamin A Deficiency: Its Prevalence and Importance as Shown by a New Test, J. Lab. & Clin. Med. **25**:149, 1939.

11. Haig, C., and Lewis, J. M.: Simple Method of Measuring Brightness Threshold of Dark Adapted Eye at All Ages, Proc. Soc. Exper. Biol. & Med. **41**:415, 1939.

12. May, C. D.: Personal communication to the authors, 1938.

13. Evelyn, K. A., and Cipriani, A. J.: A Photoelectric Micro-Colorimeter, J. Biol. Chem. **117**:365, 1937.

Data on Biophotometer Test and Values for Carotene and Vitamin A in the Blood Plasma of Seventy-One Subjects *

Subject	Light-Adapted Vision: Dial Reading	Light-Adapted Vision: Visual Threshold, Milli-Foot Candles	Dark-Adapted Vision: Dial Reading	Dark-Adapted Vision: Visual Threshold, Milli-Foot Candles	Plasma Carotene $L_{440} \times 10^3$	Plasma Vitamin A $L_{620} \times 10^3$ (Corrected)	Total Plasma Vitamin A Activity, Units per 100 Cc.
1	60	0.048	75	0.0140	164	127	399
1	53	0.082	88	0.0051	258	62	405
2	68	0.025	80	0.0096	171	51	344
2	45	0.158	93	0.0035	161	69	342
3	42	0.199	68	0.0250	187	44	365
3	42	0.199	80	0.0096	197	66	401
4	40	0.231	85	0.0064	137	56	288
4	40	0.231	90	0.0044	143	74	316
5	35	0.350	78	0.0110	172	56	349
5	40	0.231	83	0.0075	240	48	461
6	58	0.055	100	0.0020	66	62	171
6	47	0.132	100	0.0020	108	69	250
7	35	0.350	72	0.0180	78	60	190
7	35	0.350	73	0.0170	102	67	237
8	48	0.122	90	0.0045	161	80	352
8	50	0.104	92	0.0038	168	84	368
9	40	0.231	67	0.0280	102	39	212
9	42	0.199	85	0.0064	114	60	252
10	42	0.199	75	0.0140	126	62	275
11	40	0.231	70	0.0210	135	64	293
12	43	0.182	70	0.0210	166	64	347
13	32	0.440	70	0.0210	68	48	161
14	50	0.104	75	0.0140	104	50	226
15	46	0.144	85	0.0064	255	89	524
16	25	0.750	70	0.0210	108	90	269
17	35	0.350	75	0.0140	111	66	252
18	40	0.231	70	0.0210	105	54	232
19	40	0.231	78	0.0110	58	50	146
20	42	0.199	86	0.0060	122	75	280
21	35	0.350	80	0.0096	168	81	365
22	43	0.182	75	0.0140	102	75	245
23	40	0.231	75	0.0140	116	73	268
24	45	0.158	85	0.0064	161	71	344
25	42	0.199	90	0.0044	137	73	304
26	45	0.158	90	0.0014	119	59	260
27	35	0.350	80	0.0096	56	106	192
28	37	0.300	75	0.0140	66	57	166
29	35	0.350	75	0.0140	168	73	358
30	35	0.350	75	0.0140	134	73	299
31	45	0.158	75	0.0140	184	146	451
32	25	0.750	74	0.0160	84	64	204
33	30	0.510	85	0.0064	64	59	164
34	35	0.350	73	0.0170	81	94	226
35	35	0.350	75	0.0140	100	62	230
36	30	0.510	64	0.0350	58	75	169
37	32	0.440	74	0.0160	119	63	264
38	30	0.510	74	0.0160	86	57	201
39	30	0.510	91	0.0041	102	74	244
40	32	0.440	68	0.0250	102	69	239
41	8	3.200	65	0.0320	347	76	672
42	15	1.700	70	0.0210	208	85	439
43	30	0.510	68	0.0250	63	81	183
44	30	0.510	92	0.0038	155	93	354
45	43	0.182	85	0.0064	129	69	286
46	40	0.231	93	0.0035	254	95	528
47	25	0.750	75	0.0140	89	66	214
48	48	0.122	71	0.0200	111	89	373
49	50	0.104	92	0.0038	78	86	213
50	53	0.082	85	0.0064	85	43	187
51	35	0.350	88	0.0051	107	59	239
52	67	0.028	95	0.0030	109	58	242
53	38	0.275	75	0.0140	18	57	82
54	40	0.231	91	0.0041	140	105	339
55	40	0.231	88	0.0051	140	59	297
56	40	0.231	88	0.0051	155	70	333
57	50	0.104	86	0.0060	32	43	95
58	62	0.041	80	0.0096	278	58	536
59	48	0.122	85	0.0064	126	61	274
60	40	0.231	85	0.0064	104	71	245
61	47	0.132	84	0.0069	163	59	337
62	42	0.199	88	0.0051	137	47	280
63	40	0.231	80	0.0096	137	38	272
64	42	0.199	82	0.0082	128	58	275
65	38	0.275	94	0.0032	61	28	139
66	50	0.104	90	0.0044	242	58	473
67	35	0.350	70	0.021	61	71	170
68	37	0.300	80	0.0096	196	67	401
69	20	1.14	83	0.0075	92	60	214
70	40	0.231	88	0.0051	197	54	392
71	37	0.300	90	0.0044	184	91	402

* Nine subjects were examined twice, before and after being given 25,000 U. S. P. units of vitamin A daily for five days. The first line of figures for each shows the data obtained before vitamin A was given.

recorded as L_{440}. It was then evaporated to dryness in the optical cell of the same instrument; 1 cc. of 22.5 per cent antimony trichloride in chloroform was pipetted into the cell, and a reading (L_{620}) of the blue color produced by the vitamin A and the carotene was made with the 620 millimicron filter in position. The carotene and vitamin A contents of the plasma samples are recorded as L values in the accompanying table. For carotene the value of L_{440} is given as read, and for vitamin A the value L_{620} (corrected), which is $L_{620} - 0.14 \times L_{440}$ (cf. Dann and Evelyn [14]).

The total biologic activity of the plasma was calculated as follows: Since the extract derived from 0.67 cc. of plasma was present in the optical cell and the light path through the solution was 1 cm., neglecting meniscus correction one may write (equation 1):

$$L \text{ (1 per cent, 1 cm., 440 millimicrons)} = 0.015 L_{440}$$

For pure carotene this L value is 1,440 (Dann and Evelyn [14]), so that carotene is present in the plasma as the fraction $\frac{0.015\ L_{440}}{1,440}$. Transposing this expression, one has equation 2:

$$\text{Milligrams of carotene per hundred cubic centimeters of plasma} = 1.04\ L_{440}$$

The biologic activity of carotene is by definition 1.67 U. S. P. units of vitamin A per microgram, so that the activity of the carotene in the plasma is given by equation 3:

$$\text{U. S. P. units per hundred cubic centimeters of plasma} = 1,736\ L_{440}$$

For the activity of the vitamin A one may use the L value 5,000, since Holmes and Corbet [15] showed that E (1 per cent, 1 cm., 328 millimicrons) for crystalline vitamin A is 2,100, and its activity is 3 U. S. P. units per microgram, and Dann and Evelyn showed that E (1 per cent, 1 cm., 328 millimicrons corrected) = 0.41 L (1 per cent, 1 cm., 620 millimicrons). Then by similar calculations to those for carotene, the biologic activity of the vitamin A of the plasma is (equation 4):

$$\text{U. S. P. units per hundred cubic centimeters of plasma} = 900\ L_{620} \text{ (corrected)}$$

Finally, combination of equations 3 and 4 gives:

$$\text{Total biologic activity of the plasma in U. S. P. units} = 1,736\ L_{440} + 900\ L_{620} \text{ (corrected)}.$$

No allowance is made for that part of the yellow pigment which is not carotene; consequently the values for carotene will be somewhat too high. It must be noted that the constants in the equations depend on the use of the exact volumes described.

Biophotometer Readings.—All biophotometer tests were made with the standard technic recommended by Jeans and his co-workers,[7] except that after exposure to the bleaching light an interval of two and one-half minutes was allowed instead of making the next reading instantly. For comparison with the blood vitamin A we have used two of the readings obtained in the standard test: first, the reading obtained two and one-half minutes after the three minute exposure of the subjects' eyes to the bright light—the "light-adapted visual threshold," and second, the reading obtained 15 minutes after exposure to the bright light—the "dark-adapted visual threshold."

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14. Dann, W. J., and Evelyn, K. A.: The Determination of Vitamin A with the Photoelectric Colorimeter, Biochem. J. **32**:1008, 1938.

15. Holmes, H. N., and Corbet, R. E.: The Isolation of Crystalline Vitamin A, J. Am. Chem. Soc. **59**:2042, 1937.

The results obtained are collected in the table. Correlation coefficients were calculated for both the light-adapted visual threshold and the dark-adapted visual threshold in turn against the carotene content of the plasma, the vitamin A content of the plasma and the total vitamin A activity of the plasma, respectively. In view of the suggestion of Isaacs and his associates [16] that dial readings of the biophotometer may more suitably be used than the corresponding light intensities read from the maker's calibration chart, we have also recalculated all six correlation coefficients, using dial readings in place of the light intensities. For eighty pairs of figures the correlation coefficient must differ from zero by more than 0.217 to reach the 5 per cent level of significance (Fisher [17]). Three of our calculated coefficients reach this level of significance: 1. For the light-adapted visual threshold with plasma carotene, $r = +0.283$. 2. For the light-adapted visual threshold with total vitamin A activity of plasma, $r = +0.287$. 3. For dial readings at dark adaptation with plasma carotene, $r = -0.248$.

COMMENT

On the assumption that night blindness is due to vitamin A deficiency it might be expected that a suitable datum for expressing the degree of night blindness would be correlated fairly closely with the vitamin A content of the blood. Although three of the correlation coefficients which have been calculated differ significantly from zero as judged by a conventional criterion, each is so low that it indicates only a slight degree of correlation. It would be impossible to make a useful prediction of the vitamin A content of the blood from light-adapted or dark-adapted visual thresholds measured by the biophotometer or vice versa. This result confirms the finding of Steininger and her co-workers [18] that there is no correlation between biophotometer reading and the level of vitamin A in the blood. From it we deduce that the biophotometer is unlikely to prove a suitable instrument for measuring with any precision the degree of vitamin A undernutrition of the human subject. It has been criticized on other grounds by Palmer and Blumberg [19] and by Isaacs and his associates; [16] the faults suggested by these authors may be an underlying cause of the result now reported. If so, it is possible that they might be eliminated by modification of the instrument and that a correlation between biophotometer readings and the vitamin A content of the blood might then appear.

It is also possible that some alternative method of measuring dark adaptation will give data which show a closer correlation with blood

16. Isaacs, B. L.; Jung, F. T., and Ivy, A. C.: Vitamin A Deficiency and Dark Adaptation, J. A. M. A. **111**:777 (Aug. 27) 1938.

17. Fisher, R. A.: Statistical Methods for Research Workers, ed. 7, London, Oliver & Boyd, 1938.

18. Steiniger, G.; Roberts, L. J., and Brenner, S.: Vitamin A in the Blood of Normal Adults, J. A. M. A. **113**:2381 (Dec. 30) 1939.

19. Palmer, C. E., and Blumberg, H.: The Use of a Dark Adaptation Technique (Biophotometer) in the Measurement of Vitamin A Deficiency in Children, Pub. Health Rep. **52**:1403, 1937.

vitamin A. Pett [10] has developed a new visual test, and Pett and LePage [20] have reported good correlation between response to their test and the vitamin A content of the blood. There are some points about their procedures which call for comment. The photometric methods they employed in measuring the vitamin A content of the blood are open to objection, and the values they found for carotene in the plasma are very low. Calculated from equation 2, our mean value is 139 micrograms per hundred cubic centimeters. Kimble [21] reported means of 166 micrograms for men and 189 micrograms for women. Heymann [22] found from 82 to 421 micrograms per hundred cubic centimeters of plasma in normal children, and Gaehtgens,[23] 60 micrograms per hundred cubic centimeters of serum in pregnant women. Pett and LePage did not report all their figures for carotene (total vitamin A activity is given), but for 2 subjects the values 2.7 and 2.9 micrograms per hundred cubic centimeters of plasma are stated, and from the magnitude of correction applied to the vitamin A readings for the presence of carotene it is clear that these low readings are not unusual with them.

SUMMARY

Biophotometer readings and fasting blood plasma levels of vitamin A have been determined for 71 subjects; for 9 of them the readings were repeated after five days' administration of a supplement of vitamin A. Only a slight correlation was found between the biophotometer readings and the levels of vitamin A in the blood.

The mean and standard deviation for the figures per hundred cubic centimeters of plasma were; carotene, 138 ± 62 micrograms; vitamin A, 263 ± 96 U. S. P. units, and total biologic activity, 493 ± 200 U. S. P. units.

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20. Pett, L. B., and LePage, G. A.: Vitamin A Deficiency: III. Blood Analysis Correlated with a Visual Test, J. Biol. Chem. **132**:585, 1940.

21. Kimble, M. S.: Photocolorimetric Determination of Vitamin A and Carotene in Human Plasma, J. Lab. & Clin. Med. **24**:1055, 1939.

22. Heymann, W.: Carotenemia in Diabetes, J. A. M. A. **106**:2050 (June 13) 1936.

23. Gaehtgens, G.: Der Uebergang von Carotin und Vitamin A aus dem mutterlichen in den kindlichen Blutkreislauf, Arch. f. Gynäk. **164**:389, 1937; abstracted, Nutrition Abstr. & Rev. **7**:712, 1938.

DARK ADAPTOMETER READINGS OF SUBJECTS ON A DIET DEFICIENT IN VITAMIN A

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In this paper some observations on the dark adaptation of 2 subjects on a diet low in vitamin A are described, and their bearing on the use of the dark adaptometer of Hecht and Shlaer [1] as an instrument for the detection of vitamin A deficiency is discussed. This instrument is one of the most promising of those developed in the attempt to find a measure of visual dysadaptation which will serve as a reliable indicator of the state of vitamin A nutrition (compare the introduction of a paper written by Caveness, Satterfield and one of us [Dann]).[2] It meets certain specifications which are enumerated in that paper as essential for measurement of visual thresholds during the course of light and dark adaptation and which have not been met in earlier instruments.

With the new dark adaptometer Hecht and Mandelbaum [3] have examined a group of suitable subjects to establish the normal range of variation of the curve of dark adaptation under standard conditions and have observed the effect of a diet low in vitamin A on the dark adaptation of 4 subjects. They found that "the presence of a dietary avitaminosis becomes evident after the first day of the absence of vitamin A from the diet." Wald and his co-workers,[4] using a different instrument of essentially similar specifications, made observations on a single subject through a period of high vitamin A intake and a subsequent period of low vitamin A intake. They first observed a departure from normal dark adaptation on the fourth day of the deficient diet, that is to say, at a time when the subject could not be considered to be at all deficient in vitamin A according to older ideas.

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1. Hecht, S., and Shlaer, S.: An Adaptometer for Measuring Human Dark Adaptation, J. Optic. Soc. America **28**:269, 1938.

2. Caveness, H. L.; Satterfield, G. H., and Dann, W. J.: Correlation of the Results of the Biophotometer Test with the Vitamin A Content of Human Blood, Arch. Ophth., this issue, p. 827.

3. Hecht, S., and Mandelbaum, J.: The Relation Between Vitamin A and Dark Adaptation, J. A. M. A. **112**:1910 (May 13) 1939.

4. Wald, G.; Jeghers, H., and Arminio, J.: An Experiment in Human Dietary Night-Blindness, Am. J. Physiol. **123**:732, 1938.

These findings are so striking and apparently so much at variance with what is known of the mammal's ability to store vitamin A as a protection against temporary lack of dietary vitamin A that it was decided to make a similar series of observations, which are recorded here.

EXPERIMENTAL DATA

The 2 experimental subjects were in normal health at the beginning of the experimental period. M. E. Y., a woman aged 35 years, weighing 136 pounds (61 Kg.), remained in good health throughout. W. J. D., a man aged 35 years, weighing 142 pounds (64 Kg.), had severe coryza and bronchitis after two weeks on the deficient diet but otherwise remained well.

During a preliminary period of twenty days the subjects ate their usual mixed diets, in which the chief sources of vitamin A were milk fat, eggs, green and

*Data on Plasma Carotene and Vitamin A**

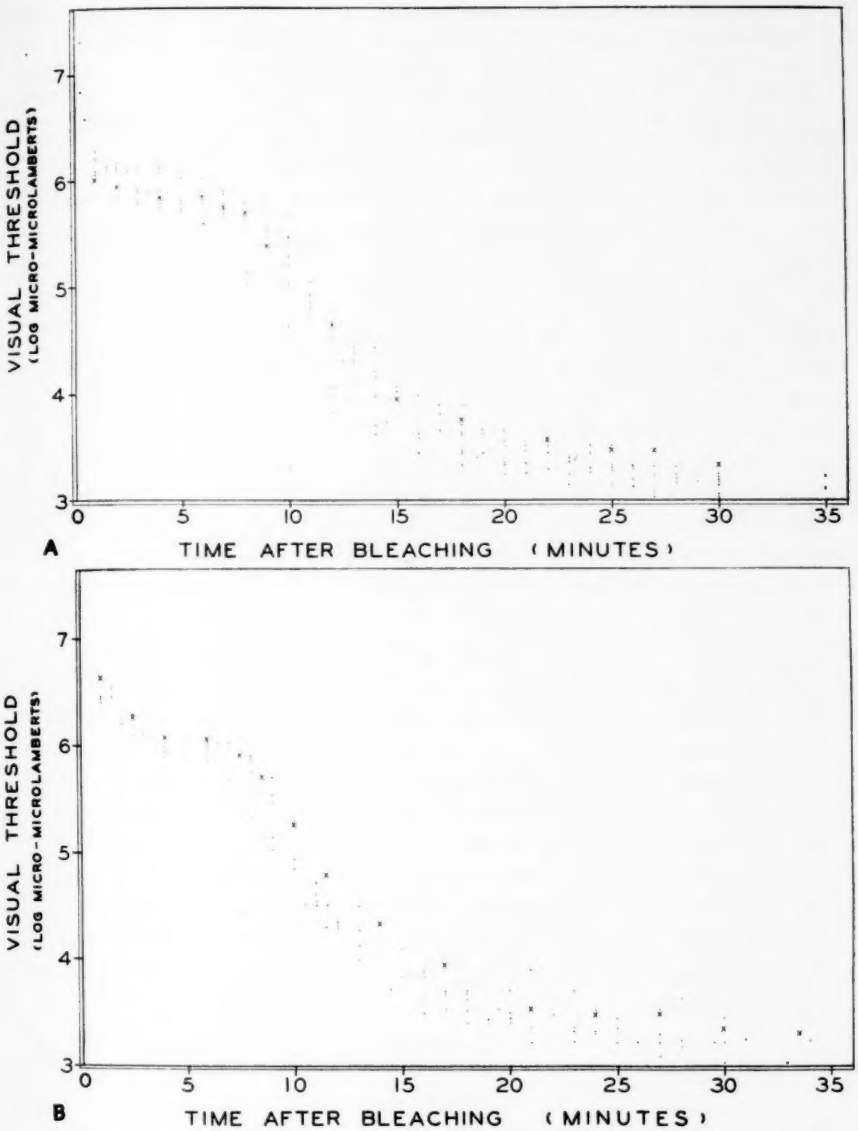
	Subject M. E. Y.		Subject W. J. D.	
Days on Deficient Diet	Carotene L 440 × 10^3	Vitamin A L 620 × 10^3 (Corrected)	Carotene L 440 × 10^3	Vitamin A L 620 × 10^3 (Corrected)
6	198	49	118	73
11	201	94	128	98
15	148	44	119	88
23	186	64		
29	160	54	122	78
34	153	45	116	88
Days After Return to Normal				
11	268	69		
18	297	81		
19	297	71		
20	280	64		
21	265	68		

* The readings were made and the results expressed exactly as in the paper by Caveness, Satterfield and Dann.[2]

yellow vegetables, fish and liver. After the preliminary period, diets low in vitamin A were taken for five weeks. For four weeks a regimen similar to that described by Wald and his associates was followed. From the mixed diet previously taken, the milk fat, eggs, fish and fat meat, glandular organs and colored fruits and vegetables were omitted. In two respects our regimen differed from that of Wald and his co-workers; no supplements of vitamin B, vitamin C or vitamin D were taken, and separated milk or buttermilk was included in the diet after control tests showed that it was free from vitamin A (no vitamin A was detected in 50 cc. by the Carr-Price test). The vitamin A content of such a diet was estimated by Wald and his associates to be less than 200 U. S. P. units daily. During the fifth week this was reduced to the vanishing point by omitting the milk to avoid any chance of a batch incompletely separated and also by omitting every article of diet which has not been reported to be free of vitamin A by biologic test. The tables of Daniel and Munsell[5] and of Fixsen and Roscoe[6] were used.

5. Daniel, E. P., and Munsell, H. E.: Vitamin Content of Foods, Miscellaneous Publication 275, United States Department of Agriculture, 1937.

6. Fixsen, M. A. B., and Roscoe, M. H.: Tables of the Vitamin Content of Human and Animal Foods, Nutrition Abstr. & Rev. **7**:823, 1938.



Data on the dark adaptation of the 2 subjects (*A*, M. E. Y., and *B*, W. J. D.). In each chart the dots represent single points on the curves of dark adaptation measured on eight occasions over a thirty day preliminary period on a normal diet. The spread of the dots may be taken to indicate the normal variation of the dark adaptation curve. (Compare the curves in figure 1 of Mandelbaum and Hecht.[9])

The crosses indicate points determined for the dark adaptation curve on the thirty-fifth day of subsistence on a diet deficient in vitamin A. Their position shows no significant deviation from the normal.

Curves of dark adaptation were taken at intervals by the standard procedure described by Hecht and Mandelbaum.[3] The results obtained are shown in the chart. Fasting blood samples were taken each time a dark adaptation curve was obtained after the first eight days on the deficient diet, and the vitamin A content was estimated by the method of May.[7] (For details see the aforementioned paper).[2] The data on the blood are given in the accompanying table.

COMMENT

It is evident that our results with the adaptometer are diametrically opposite to all those previously described in detail by Hecht and his co-workers and by Wald and his associates. Hecht and Mandelbaum,[3] reporting on 4 subjects, stated that after the change from the habitual diet to a diet deficient in vitamin A the power of dark adaptation was measurably impaired within twenty-four hours, the degree of impairment increasing continuously during the thirty days that the subjects were on the deficient diet. Wald and his co-workers[4] reported on 1 subject, who was repeatedly examined during a preliminary control period on a normal diet supplemented by 70,000 U. S. P. units of vitamin A daily. The dark adaptation of this subject was nevertheless found to be impaired on the fourth day of diet deficient in vitamin A. Our results show no significant change in the 2 subjects after thirty-five days on a similar deficient diet. In a more recent paper Wald and Steven[8] described a repetition of the work of Wald and his associates on another subject, with similar results, but they also stated without further discussion that "on an identical regime and within comparable periods about half of our subjects develop no night blindness at all. It seems to have little to do with the vitamin A reserve since all our subjects have been saturated with vitamin A before beginning the deficient diet." Mandelbaum and Hecht[9] have given a preliminary report of an extension of their study to 17 subjects, of whom 14 showed immediate impairment of dark adaptation on changing to a deficient diet and the other 3 did not show any impairment until four to twelve weeks after the change in diet.

It is now evident that the disagreement between our results and those of Booher and his co-workers[9a] and the results first published by Wald and Hecht is resolved by the discovery that impairment of dark adaptation appears in some subjects immediately after depriva-

7. May, C. D.: Personal communication to the authors, 1938.

8. Wald, G., and Steven, D.: An Experiment in Human Vitamin A-Deficiency, Proc. Nat. Acad. Sc. **25**:344, 1939.

9. Mandelbaum, J., and Hecht, S.: Dark Adaptation Under Controlled Dietary Vitamin A Conditions, Am. J. Physiol. **129**:416, 1940.

9a. Booher, L. E.; Callison, E. C., and Hewston, E. M.: An Experimental Determination of the Minimum Vitamin A Requirements of Normal Adults, J. Nutrition **17**:317, 1939.

tion of vitamin A, while others suffer no impairment for a considerable time. In either case there can be no question of immediate vitamin A deficiency; therefore, we conclude that because change in the power of dark adaptation occurs in some subjects without vitamin A deficiency such changes cannot be used in the diagnosis of mild vitamin A deficiency. The immediate change observed in some subjects is difficult to explain. It is well established that the mammal is able to amass large stores of vitamin A in the body and subsequently to withstand long periods of a vitamin A–deficient diet without showing deficiency symptoms.[10] Holm [11] has shown that in rats restricted to a deficient diet night blindness did not develop until the lapse of three weeks, although xerophthalmia (a sign of severe deprivation) appeared in four weeks. It is therefore unexpected that a human being should show an immediate onset of night blindness, however slight, after being deprived of vitamin A. This is especially true of the subjects observed by Wald and his collaborators,[4] who had been given such large amounts of vitamin A immediately before the experiment began that the authors were able to establish firmly that a subnormal power of dark adaptation as measured with the dark adaptometer can occur when the subject is not deficient in vitamin A. This conclusion is strengthened by the finding of Hecht and Mandelbaum that when their subjects returned to a normal diet and supplemented it with 50,000 U. S. P. units of vitamin A daily the dark adaptation did not become normal for two months.

The difference between persons who do and those who do not have immediate night blindness when deprived of vitamin A may perhaps be accounted for if some can utilize body stores of vitamin A during administration of a deficient diet while others cannot. Similarly, the disparity in the rate of return to normal after taking vitamin A may be due to individual variation in ability to transfer vitamin A from the blood stream to the retina. Evidence must be sought to decide these points. Meanwhile it is necessary on the basis of all the recorded experience with the adaptometer to conclude that this instrument is not a reliable tool for the detection of mild avitaminosis A.

The whole question of normal vitamin A nutrition needs reexamination in view of the observations that impaired dark adaptation may appear within four days of decreasing the vitamin A intake from 70,000 to about 100 U. S. P. units daily and that recovery from night blindness may take two months when the daily intake of vitamin A is increased

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10. Moore, T.: The Distribution of Vitamin A and Carotene in the Body of the Rat, Biochem. J. **25**:275, 1931. McCoord, A. B., and Luce-Clausen, E. M.: The Storage of Vitamin A in the Liver of the Rat, J. Nutrition **7**:557, 1934.

11. Holm, E.: Demonstration of Hemeralopia in Rats Nourished on Food Devoid of Fat-Soluble-A-Vitamin, Am. J. Physiol. **73**:79, 1925.

to 50,000 U. S. P. units. In the light of present knowledge it is scarcely possible to regard a whole human organism as deficient in vitamin A, in however small degree, within a few days after the end of a period of forty-eight days during which 70,000 U. S. P. units of vitamin A was taken daily. If a small departure from the lowest observed dark-adapted light threshold can be detected so soon, it would seem logical to define normal vitamin A nutrition in terms of the eye as a state in which the dark-adapted eye reaches some defined level of visual threshold higher than the lowest obtainable. The lowest obtainable threshold might then be regarded as supernormal, owing to excess vitamin A.

No significant change in the vitamin A level in the plasma occurred in either of our subjects. This seems to indicate that no deficiency occurred during the period of observation and suggests that a constant supply was carried to the eyes.

SUMMARY

Two subjects failed to show night blindness measurable by the dark adaptometer of Hecht and Shlaer after five weeks on a diet deficient in vitamin A.

This finding is discussed, together with others recorded in the literature, and the conclusion is drawn that the dark adaptometer is not at present a reliable indicator of slight degrees of avitaminosis A.

ADDENDUM

Since this paper was prepared the method of vitamin A determination has been published.[12] There has also appeared the full description of the work of Mandelbaum and Hecht.[13]

A grant in aid of this study was made by the Duke University Research Council.

12. May, C. D.; Blackfan, K. D.; McCreary, J. F., and Allen, F. H., Jr.: Clinical Studies of Vitamin A in Infants and in Children, Am. J. Dis. Child. **59**: 1167 (June) 1940.

13. Mandelbaum, J., and Hecht, S.: Dark Adaptation and Experimental Human Vitamin A Deficiency, Am. J. Physiol. **130**:651, 1940.

EFFECTS OF SOME SILVER SALTS ON THE EYE

(SILVER NITRATE, SILVER AMMONIUM NITRATE, SILVER AMMONIUM SULFATE, SILVER AMMONIUM LACTATE AND A MIXTURE OF SILVER AMMONIUM NITRATE AND SILVER AMMONIUM SULFATE)

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AND

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The use of silver and its salts as therapeutic agents undoubtedly antedates the inclusion of silver nitrate in a pharmacopeia published in Rome in 69 B. C.[1] The use of silver nitrate as a medicinal agent by Geber and the Mohammedan school established by him is clearly indicated.[2] Since his time there have been numerous references to the employment of silver medicinally in a variety of ways, particularly by Avicenna, by Paracelsus in the middle of the sixteenth century and by many others up to the present time. In fact, a general survey indicates that there are few if any known physiologic impairments for which silver in some form has not been recommended. As a caustic, silver nitrate was apparently first used in the sixteenth century. Angelo Sala in 1614 reported the first case of clearly diagnosed generalized argyria.[3] He administered silver nitrate internally, probably as a purge, as a counterirritant or for the treatment of diseases of the brain. Since this first report, hundreds of cases of generalized and local argyria have been discussed in the literature.[3]

Just how long silver has been used as a therapeutic agent for local application to the eye is not known, but Avicenna in 980 A. D. first

From the Division of Pharmacology, Food and Drug Administration, Federal Security Agency.

1. Custom, C. G.: History of Medicine, New York, Alfred A. Knopf, 1926, p. 216.

2. Gager, L. T., and Ellison, E. M.: Generalized (Therapeutic) Argyria: Case Report with Necropsy and Notes on Diagnosis and Prevention, Internat. Clin. **4**:118-132 (Dec.) 1935.

3. Hill, W. R., and Pillsbury, D. M.: Argyria: The Pharmacology of Silver, Baltimore, Williams & Wilkins Company, 1939.

described discoloration of the eye due to silver, and Junge [4] in 1857 was the first to study histologically the tissues of the eye into which silver nitrate had been locally introduced, at which time the term "argyrosis" (argyria of the eye) was first used by him. The cases of "argyrosis" outnumber 3 to 1 the combined cases of all other reported forms of argyria, and it is probable that discoloration of the eye is the first objective sign of generalized argyria. Significant cosmetic disfiguration is caused by silver deposits in the eye, and any attempt to remove such discoloration is hazardous. There is evidence to indicate that disturbance of vision may result when silver is deposited in the eye, particularly if the deposition occurs in the cornea.[3] The tissues which have been reported to be affected by "argyrosis" are the conjunctiva, Descemet's membrane in the cornea, the elastic tissue, the blood vessels, the lymph spaces throughout the eye and the sheath of the optic nerve. The most important deposits seem to be localized about the blood vessels and in the elastic tissue and accessory structures. The time required for the production of "argyrosis" is variable and probably dependent on several factors, as is evidenced by an examination of the cases reported in the literature. Some of the factors involved are the nature of the silver salt used, the frequency of use, the concentrations of the solutions used and the condition of the eye subjected to treatment.

Probably the most extensive modern application of silver salts as a therapeutic agent is the use of silver nitrate in the prevention of ophthalmia neonatorum. It is required by law in many countries and in most of the United States. By far the most common strength employed is a 1 per cent solution, although 0.5 per cent and 2 per cent solutions are occasionally used. It has been observed that if the stronger solutions are used not more than 1 drop should be instilled, as a rather severe reaction may follow the use of those strengths if there has been failure subsequently to neutralize completely, by use of saline solution, all of the caustic agents.[5] That the use of a 1 per cent solution is not unattended by danger is evident, since Lehrfeld [6] stated that the use of 1 per cent silver nitrate in the eyes of 106 babies produced moderate to severe irritation in the majority of the cases. Many instances have been

4. Junge, E.: Ophthalmologisch-mikroskopische Notizen, Arch. f. Ophth. (pt. 2) **5**:191-204, 1859.

5. Credé Method and Vision, Queries and Minor Notes, J. A. M. A. **103**: 777 (Sept. 8) 1934. Silver Nitrate Solution for Instillation in Eyes of New-Born, Foreign Letters, ibid. **109**:1137 (Oct. 2) 1937.

6. Lehrfeld, L.: Limitations of Use of Silver Nitrate in Prevention of Ophthalmia Neonatorum: Report of a Survey of Nearly Twenty-Eight Thousand Hospital Birth Records and Two Thousand Cases of Ophthalmia Neonatorum, J. A. M. A. **104**:1468-1469 (April 27) 1935.

reported of severe injury and even blindness resulting from the accidental use of stronger solutions.[7]

The first use of silver salts for cosmetic purposes has probably not been recorded, but they are nearly always referred to in books on hair dyes and hair dyeing. However, the dangers attending their use have often been pointed out; for example, by Redgrove and Bare-Woollss,[8] in speaking of the New York regulation prohibiting dyes containing metallic salts other than those containing less than 5 per cent by weight of silver nitrate, made the following statement: "The latter regulation seems somewhat anomalous, as the danger of blindness from silver appears to be as great, if not greater, than with compounds of other metals. Apart from the question of possible irritation, silver forms a very opaque, insoluble compound with keratin, so that if any of the dye should fall into the eye, there is danger of it blackening the cornea and outer skin and thus causing blindness. Moreover, even if, in the course of time, the blackened area is replaced by the normal process of repair, there still remains the danger of the cornea losing its complete transparency." They spoke of the dyeing of the eyelashes as "a very dangerous procedure" and stated further: "No satisfactory guards for the eyes during lash-dyeing have yet been made. . . . *The dye must not touch the lid itself.*"

For the purpose of dyeing the hair, eyelashes, eyebrows and beard, the principal salts of silver used are silver nitrate and silver ammonium nitrate. Other salts have been used, particularly silver ammonium sulfate in a mixture with silver ammonium nitrate. When silver nitrate alone is used for coloring the hair the reaction is rather slow, and hence it is most commonly used in conjunction with pyrogallol. Likewise, pyrogallol is used with the silver ammonium salts.

In a search of the literature we have found that there are few reports other than those concerning clinical cases which describe the effects of silver nitrate on the eye, and we have not found a single report of an investigation of the effects of silver ammonium nitrate and silver ammonium sulfate. This lack of information and the extensive use of these substances in eyelash and eyebrow dyes have induced us to carry out the experiments reported in this investigation.

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7. Fejer, F. J.: Cauterization of Cornea Due to Ten per Cent Solution of Silver Nitrate, Med. Klin. **22**:886-887 (June 4) 1926. Blindness Following Prophylactic Use of Silver Nitrate Solution, Foreign Letters, J. A. M. A. **77**:802 (Sept. 3) 1921. Distribution of Silver Nitrate by the State, Medical News (Virginia), ibid. **87**:857 (Sept. 11) 1926. Boström, C. G.: Application of Credé's Prophylactic Method, Acta obst. et gynec. Scandinav. **5**:355-362, 1926.

8. Redgrove, H. S., and Bare-Woollss, J.: Hair Dyes and Hair-Dyeing Chemistry and Technique, London, William Heinemann, Ltd., 1939.

TABLE I.—*Summary of Effects of the Instillation of Various Solutions of Different Concentrations into the Eyes of Rabbits*

No. of Animals Used	Concentration of Solutions, per Cent *	Hyperemia †	Swelling †	Mucopurulent Exudation †	Coagulation †	Scar Tissue Formation †	Corneal Injury ‡	Duration, Days §	Comment (Numbers in Parentheses Indicate Number of Animals)
					Silver Nitrate				
4	12	3-4	4	3-4	2-4	2-3	Hazy to opaque	7-9	Blindness (1); silver deposits (1)
5	6	3-4	3	2-3	1-2	None	Clear to cloudy	4-6	See individual columns
4	4	2-4	2-3	1-2	0-1	None	Clear	4-6	See individual columns
10	2	2-4	1-4	1-3	0-1	None	Clear to cloudy	2-9	Eye of one animal healed slowly; majority required five days
3	1.5	2-4	1-3	2-3	None	None	Clear	2-3	See individual columns
6	1	2-3	1-2	1-2	0-1	None	Clear to hazy	2-4	See individual columns
					A Mixture of Silver Ammonium Nitrate and Silver Ammonium Sulfate				
22	12	3-4	3-4	3-4	3-4	2-4	Cloudy to opaque	20 to permanent	Blindness (7); silver deposits (8); ulcerations and rupture of ball (2); severe adhesions (11)
6	6	3-4	3-4	3-4	2-3	2-3	Cloudy to opaque	27 to permanent	Blindness (1); silver deposits (3); severe adhesions (3)
2	12, ½ drop	4	4	4	3	2	Opaque	36 to permanent	Silver deposits, adhesions and permanent distortion of lids
2	12, ⅕ drop	4	3	3	3	3	Very cloudy	36 to permanent	Silver deposits, adhesions and permanent distortion of lids
					Silver Ammonium Nitrate				
4	12	4	4	4	4	3	Opaque	20 and permanent	Silver deposits (4); corneal scar; adhesions; blindness in two animals
2	12, ½ drop	3	2	2	1	2	Cloudy	20 and permanent	Scar tissue and silver deposit
8	6	3-4	3-4	3-4	2-3	1-2	Cloudy	9-12	Silver deposits (2); ulceration (3); adhesions (1); granulation of lids (1)
2	6, ½ drop	3	3-4	1-2	1-2	None	Cloudy	9	See individual columns
12	4	2-4	1-4	1-3	1-3	0-3	Hazy to cloudy	4-10	Some permanent injury
16	2	3-4	3-4	1-4	1-2	0-2	Clear to cloudy	5-12	Some permanent injury
6	1.5	3-4	2-4	3-4	1	None	Clear to hazy	4-5	See individual columns
4	1	3	1-2	1-3	None	None	Clear	2-3	See individual columns
					Silver Ammonium Sulfate				
2	12	4	4	3	4	4	Cloudy	20 and permanent	Blindness (2); adhesions (2); silver deposits (2)
2	12, ½ drop	3	2	2	2	2	Cloudy	12	Adhesions (2); silver deposits (2)

2	6	4	2	1	3	2	Cloudy	10	Scar tissue only permanent injury
2	6, ½ drop	2	1	1	1	None	Hazy	2	See individual columns
15	4	3-4	3-4	2-3	1-3	1-3	Hazy to very cloudy	6-19 and permanent	Injuries variable with some scar tissue in all cases, with permanent corneal injury in 2 animals; silver deposit (2)
2	2	1-2	2	1	1	None	Hazy	4	See individual columns
							Silver Ammonium Lactate		
2	12	4	4	3	4	4	Very cloudy	20 and permanent	Blindness (2) silver deposits (2); adhesions (2)
2	12, ½ drop	4	2	3	4	2	Very cloudy	20 and permanent	Blindness (1); silver deposits (2); adhesions (2)
2	6	2-4	4	2-3	1-2	2	Very cloudy	11	See individual columns
2	6, ½ drop	3	1	1	1	None	Hazy	6	See individual columns
4	2	2-4	0-1	1	0	None	Clear	5	See individual columns
							Ammonium Hydroxide		
2	3.5	4	3-4	3	3	3	Very cloudy	7-15	Ulcerations of nictitating membranes, balls and lids
2	1.75	4	3-4	2	1-2	1	Cloudy	6	Ulceration of lids
5	0.88	4	3-4	2-3	1-2	None	Cloudy	3-7	Ulceration of lids
2	0.44	2	1	Nonpurulent	None	None	Clear	2	See individual columns
							Distilled Water		
3	One drop	2	None	Watery	None	None	Clear	1-2	More effect than with boric acid or saline (see text)
							Boric Acid		
3	3	0-1	None	None	None	None	Clear	0-1	No effect
							Sodium Chloride		
4	0.85	None	None	None	None	None	Clear	0	No effect

* In the case of silver salts other than silver nitrate the concentrations given indicate that the solution contained an amount of silver equal to that in a silver nitrate solution of the percentage concentration specified.

† These conditions are evaluated as follows: 0 = no observed changes; 1 = mild changes or a small amount; 2 = moderate changes or a moderate amount; 3 = severe changes or a large amount, and 4 = intense changes or an enormous amount.

‡ The various degrees of alteration of the appearance of the cornea have been indicated as "clear," meaning no visible change, "hazy," "cloudy," "very cloudy" and "opaque."

§ The time recorded in days in this column refers only to the time required for the healing process and has no reference to scar tissue, adhesions or blindness, all of which can be considered permanent forms of injury; yet the first two may not interfere with vision and in most cases did not.

PROCEDURE

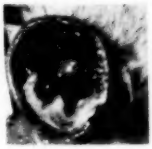
The animals used in the experiments were pure albino rabbits from several different sources. They had not been previously used for investigative purposes. They weighed from 1.5 to 3 Kg. and were considered young adults. The exact ages were not known. They were housed in air-conditioned quarters at relatively constant temperature and humidity and maintained on a standard stock diet. They were kept in individual cages which were cleaned daily and sterilized at regular intervals.

In all cases reported here the material was administered by instilling ⅕ to 1 drop of the solution into the lower cul-de-sac. Two to five minutes later in most cases a lavage of 1 per cent boric acid was used in the eye. The left eye was always used for treatment, the right eye serving as a control. The concentrations of the solutions varied in strength from 1 to 12 per cent, calculated on the basis of silver nitrate. In those cases in which highly concentrated solutions were used observations were made twice daily, and in all instances at least one examination was made every twenty-four hours. In addition to using the right eye of the animal as a negative control, we used some positive controls in order to estimate what part the treatment and manipulation necessary to make observations might play in causing injury. For this purpose one group of animals received distilled water; another, 3 per cent boric acid, and another, an 0.85 per cent saline solution. In all of these animals the results were negative or there was mild hyperemia, the distilled water being the greatest offender, indicating that osmotic properties may play some part. Another positive group of controls were treated with ammonium hydroxide. The concentrations of ammonia were 0.44 per cent, 0.88 per cent, 1.75 per cent and 3.5 per cent. The solutions of ammonium hydroxide containing less than 1 per cent of ammonia produced an injury approximately equivalent to that caused by 2 per cent silver nitrate, and solutions of greater concentrations of ammonia caused injuries comparable to those observed after administration of 6 per cent silver nitrate. It will be noted that in these experiments we have considered the sequence of events as follows: hyperemia, swelling, mucopurulent exudation, coagulation, scar tissue formation and corneal injury. We have also noted the duration of these conditions, and we have attempted to evaluate all these factors, as is explained in the footnote to the table. In the case of the mixture of silver ammonium nitrate and silver ammonium sulfate, the 12 per cent concentration consisted of 4.5 per cent silver nitrate and sufficient silver sulfate to make the equivalent of 12 per cent silver nitrate. In the case of the silver ammonium nitrate, silver ammonium sulfate and silver ammonium lactate, the various strengths of solutions were prepared so that they contained an amount of silver equivalent to that contained in a silver nitrate solution of the strength indicated. For example, when it is stated that 12 per cent silver ammonium lactate was used, it is meant that a silver ammonium lactate solution was made up so that the concentration of silver in the solution would be the same as in a 12 per cent silver nitrate solution. A summary of the results is presented in the accompanying table.

COMMENT

When solutions of silver salts were placed in the eyes of rabbits there was an immediate response from the animal indicating some degree of pain, followed immediately by intense lacrimation. The degree of pain indicated paralleled the concentrations of salts used. There was also immediate formation of a white precipitate, which in all cases consisted in

A



B

C

A, normal eye of a rabbit held open, showing the nictitating membrane. *B*, rabbit's eye twenty-four hours after treatment with ½ drop (0.025 cc.) of a solution of a mixture of 4.5 per cent silver nitrate and sufficient silver sulfate to make the equivalent of a 12 per cent silver nitrate solution as the silver ammonium salts, the solution containing not more than 0.1 per cent excess ammonia. *C*, rabbit's eye twenty-four hours after treatment with ½ drop (0.025 cc.) of a 12 per cent solution of silver nitrate as silver ammonium nitrate, the solution containing not more than 0.1 per cent excess ammonia.

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part of silver chloride; however, with high concentrations of silver in the solution under investigation the chloride content of the secretions of the eye was, of course, not sufficient to prevent a large portion of the administered silver ions from access to the tissues of the eye, in which case they reacted with those tissues, forming opaque silver combinations with the proteins. When the eyes were subsequently washed with boric acid solutions, these opaque films and heavier deposits were not removed. In most cases it was principally the protein of the conjunctival membrane which had been injured, but in many instances in which the higher concentrations were used the caustic action of the silver salt was such as to remove the conjunctival membrane entirely. In these cases, in the denuded areas, the silver ions attacked the underlying tissues and often caused the formation of heavy scar tissue on the eyelids and eyeballs. In many cases the injury to the cornea was so severe that blindness resulted. In other cases there was no visible denudation of the eyeballs and eyelids and yet there were injury to the underlying tissues and even the formation of heavy scar tissue. In some instances the injury to the cornea was so severe that the eyeball ruptured. After several days black deposits occurred on the eyeballs of many of the rabbits. These black deposits appeared even in cases in which dilute solutions had been used.

A consideration of the results presented in the table enables one to make the following comparisons:

1. A solution of 12 per cent silver nitrate can be compared with (*a*) an equimolecular solution of a mixture of silver ammonium nitrate and silver ammonium sulfate; (*b*) an equimolecular solution of silver ammonium nitrate; (*c*) an equimolecular solution of silver ammonium sulfate, and (*d*) an equimolecular solution of silver ammonium lactate. The results indicate clearly that solutions of ammonium salts as measured by amounts of scar tissue, duration of injury and blindness which they produce are much more injurious than is a solution of silver nitrate. This is undoubtedly due to the fact that the silver ammonium salts are very reactive, so that when they come in contact with the fluids and tissues of the eye silver ions and ammonia are immediately released. The liberated ammonia is itself a strong irritant, injuring the tissues of the eye to some extent. More important, however, it seems to us from the results (which we have indicated as clearly as possible by the data presented in the table) is the fact that the tissues after irritation by the ammonia are more receptive to the injurious effects of the silver ions. If this is not true, the only alternative would seem to be that the silver ammonium ion itself is the offending agent. However, we believe that the silver ammonium ion is so unstable that the first explanation is to be preferred. It seems well to point out that, from the available evidence from the literature and from experiments carried out in this laboratory,

the silver in the silver ammonium solutions is as readily available for chemical reaction and physiologic activity as is the silver in a silver nitrate solution, if not more so.

2. The results with the solutions equivalent in silver content to a 6 per cent solution of silver nitrate when considered in the same manner indicate just as clearly that the silver ammonium salts are far more injurious than the simple silver nitrate solution.

3. At the 4 per cent levels comparisons are possible only in the cases of silver nitrate, silver ammonium nitrate and silver ammonium sulfate. The evidence is still clear that the most injurious effects are caused by the silver ammonium salts.

4. At the 2 per cent and 1 per cent concentrations (when comparisons are possible) the differences are not so striking, because the injuries are not so severe and comparisons are more difficult to make.

5. When the results presented in the table are carefully considered, the most outstanding fact is that on the basis of scar tissue formation and the duration of the time required to heal the 4 per cent solutions of the silver ammonium salts were just as deleterious to the tissues of the eye as the 12 per cent solution of silver nitrate and that by all standards of comparison the 6 per cent solutions of silver ammonium salts were just as injurious as the 12 per cent silver nitrate, even to the extent of causing blindness.

6. Another observation (recorded in the table) made during this investigation was the fact that when ½ drop or even ⅕ drop of a concentrated silver salt solution was used the injurious effects were more severe than when the same amount of the silver salt was used in a more dilute solution. This would indicate that concentration is an important factor to be considered in this instance, as is well recognized in the case of many other toxic and injurious substances.

In the minds of some who are not familiar with the solubility of silver sulfate the question may arise why this substance was not compared with silver nitrate and the ammonium salts. The answer is, of course, that it is too insoluble, having a solubility of less than 1 per cent at room temperature. It is our opinion that the action of all silver salts depends on the availability of the silver ion, which can be accessible only when the salts are in solution. This is true whether one is considering the corrosive and deleterious effects on the delicate tissues of the eye or whether one is considering the dyeing of the hair. An observation which should probably not be passed without comment was the number of instances in which silver deposits were observed. The deposits referred to in the table are only those which were seen on the eyeball and ranged from very small to very large. It should be kept in mind that these all occurred after a single application of the silver salt to the eye and that

the deposits were always more intense in the lids. Noticeable scar tissue was also more abundant in the lids.

SUMMARY AND CONCLUSIONS

The physiologic effects of solutions of the following substances have been observed on the eyes of rabbits: silver nitrate (1 to 12 per cent); a mixture of silver ammonium nitrate and silver ammonium sulfate (equivalent in silver content to 6 per cent and 12 per cent solutions of silver nitrate); silver ammonium nitrate (equivalent to 1 to 12 per cent solutions of silver nitrate); silver ammonium sulfate (equivalent to 2 to 12 per cent solutions of silver nitrate); silver ammonium lactate (equivalent to 2 to 12 per cent solutions of silver nitrate); ammonia (0.44 to 3.5 per cent); boric acid (3 per cent); sodium chloride (0.85 per cent), and distilled water.

Comparative effects were noted in all instances after the administration of a single measured drop in the lower cul-de-sac of the left eye, the right eye serving as a control. In some instances $\frac{1}{5}$ or $\frac{1}{2}$ drop was used.

When the silver concentrations were the same the results clearly showed that silver ammonium salts are more injurious than silver nitrate.

Extensive scar tissue formation and even blindness often resulted from the use of silver ammonium salts of equivalent in silver content to 6 per cent and 12 per cent solutions of silver nitrate. In 1 of 4 cases blindness resulted when 12 per cent silver nitrate was used.

Silver ammonium salt solutions equivalent in silver content to 6 per cent and even 4 per cent solutions of silver nitrate are apparently as deleterious to the tissues of the eye as 12 per cent silver nitrate.

Ammonia solutions of 3.5 per cent concentration caused extensive damage to the eyes, and even an 0.88 per cent solution caused severe irritation which required several days for recovery.

Boric acid (3 per cent) and salt solution (0.85 per cent) caused no effects, while the effects produced by distilled water (probably osmotic) were just noticeable.

Silver salts in all the concentrations used were irritating to the eyes of rabbits, the degree of irritation being dependent on the concentration used and also to a great extent on the nature of the salt being tested.

The greater corrosive and deleterious effects of the silver ammonium salts probably represent a summation and combination of the effects of the ammonium ion and the silver ion liberated by the reaction of these salts with the constituents of the fluids and tissues of the eye.

Dark silver deposits can result from a single application of silver salts to the eye.

Silver salts should not be used in the eye except when absolutely necessary, and even then extreme care should be exercised.

SYMPATHETIC OPHTHALMIA CAUSED BY NON-PERFORATING INTRAOCULAR SARCOMA

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From the publication of the earliest description of sympathetic ophthalmia to the present day, many articles have been written on this interesting subject. With all the knowledge of the disease, the exact cause is still unknown. The vast majority of articles and case reports attribute the predisposition to the disease to trauma, usually the perforating variety. Little credence has been given to a nontraumatic origin.

In a recent article Irvine [1] stated that "no record was found at the Massachusetts Eye and Ear Infirmary of sympathetic ophthalmia occurring without there having been operative or traumatic perforation of the globe prior to its onset." He further stated: "There are reports in the literature describing sympathetic uveitis in sarcomatous eyes without perforation. The rarity of these indicates that further confirmation of the absence of perforation or operative intervention is needed." This point is well made, as even a serial section of the globe cannot prove a perforation if a section is made through the exact site of a minute perforation.

The purpose of this paper is to review the literature to date, eliminating all cases in which there is any suspicion of surgical, traumatic or doubtful origin of the condition, and presenting only the thoroughly studied and carefully recorded authentic cases as far as possible. To this series we add a case of our own. In all these cases there was no perforation of the globe in any portion, either from within or from without.

In 1936, Peters [2] reviewed the cases reported and the literature published until October 1935 and summarized his analysis, excluding

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From the Army Medical Museum.

Presented before the Buffalo Ophthalmological Society, Dec. 12, 1940.

1. Irvine, R.: Sympathetic Ophthalmia: Clinical Review of Sixty-Three Cases, Arch. Ophth. **24**:149 (July) 1940.

2. Peters, A.: Die sympathische Augenerkrankung. Literaturbericht 1919 bis Oktober 1935, Berlin, S. Karger, 1936.

the cases of Deutschmann [3] and Nieden [4] because at the time of their publication the histologic character of sympathetic ophthalmia was not clear. The 3 cases of Fuchs [5] and the 1 each of Meller [6] and Reis [7] were considered authentic. Peters cited Morax's review [8] and briefly analyzed the cases reported by Daniels,[9] Lawford,[10] Deutschmann,[3] Nieden,[4] Milles,[11] Reis,[12] Meller,[6] Schwartz,[13] Butler and Evans,[14] Delaney,[15] Tooker and Lamb [16] and Redslob.[17] The conclusion reached was that only 2 cases can be accepted; however, Fuchs's cases were not mentioned. The reports are conflicting and contradictory; therefore, only those cases which meet our requirements will be briefly reviewed, and comment will be made on those conflicting reports which merit consideration.

Fuchs,[5] in a lengthy discussion of sympathetic ophthalmia based on 35 cases, reported that in 3 cases the condition was due to sarcoma of

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3. Deutschmann, R. H.: Ueber die Ophthalmia migratoria (sympathische Augenentzündung), Leipzig, L. Voss, 1889.

4. Nieden, A.: Ueber sympathische Entzündung infolge von Sarkom der Choroidea, Arch. f. Augenh. **29**:339, 1894; cited by Morax.[8]

5. Fuchs, E.: Ueber sympathisierende Entzündung (nebst Bemerkungen über seröse traumatische Iritis), Arch. f. Ophth. **61**:365, 1905.

6. Meller, J.: Intraoculares Sarkom und sympathisierende Entzündung, Arch. f. Ophth. **72**:167, 1909.

7. Reis, W.: Zur Frage nach dem histologischen und äetiologischen Charakter der sympathisierenden Entzündung, Arch. f. Ophth. **80**:69, 1911.

8. Morax, V.: L'ophtalmie sympathique peut-elle se développer sans perforation ni rupture des membranes oculaires? Ann. d'ocul. **169**:637, 1932.

9. Daniels: Zur Frage der sympathischen Ophthalmie bei Aderhautsarkomen, Ztschr. f. Augenh. **74**:146, 1931; cited by Morax.[8]

10. Lawford, J. B.: Cases of Intra-Ocular Sarcoma, Roy. London Ophth. Hosp. Rep. **11**:400, 1887; cited by Morax.[8]

11. Milles, W. J.: Two Cases of Intra-Ocular Sarcoma, Producing Sympathetic Ophthalmitis, Roy. London Ophth. Hosp. Rep. **11**:43, 1886; cited by Morax.[8]

12. (*a*) Reis.[7] (*b*) Flächen Sarkom der Aderhaut und sympathisierende Eutzündung, Ber. ü. d. Versamml. d. Ophth. Gesellsch. (1910) **36**:351, 1911; cited by Morax.[8]

13. Schwartz, F.: Melanosarcoma of the Choroid; Sympathetic Ophthalmia; Retrobulbar Neuritis, Am. J. Ophth. **10**:35, 1927.

14. Butler, H., and Evans, J.: A Case of Sympathetic Inflammation Associated with Intraocular Sarcoma, Brit. J. Ophth. **11**:230, 1927; cited by Morax.[8]

15. Delaney, J. H.: Sympathetic Ophthalmia Unassociated with Perforation or Rupture of Eyeball, Arch. Ophth. **5**:781 (May) 1931; cited by Morax.[8]

16. Tooker, C. W., and Lamb, H. D.: Irido-Cyclitis Sympathica Following an Iridectomy for Glaucoma Secondary to Sarcoma of the Choroid, Arch. Ophth. **53**:439, 1924; abstracted, Klin. Monatsbl. f. Augenh. **73**:814, 1924; cited by Peters.[2]

17. Redslob, E.: Tumeur de la choroïde et ophtalmie sympathique, Bull. Soc. d'opht. de Paris, 1933, p. 268; abstracted, Zentralbl. f. d. ges. Ophth. **31**:53, 1934; cited by Peters.[2]

the choroid. Of these, only 2 meet our specified requirements. In the first (case 33), a 40 year old woman with a blind right eye sixth months later had an inflamed left eye (chronic uveitis). The right eye was removed and on section proved to contain a melanosarcoma. The end result for the left eye was vision limited to finger counting at 3 meters and seclusio pupillae. There was no history of injury or trauma. In the second (case 34), a 42 year old man had a detached retina in the right eye. Two months later the eye became blind. Five weeks later the left eye became involved. The right eye was enucleated, but the condition in the left eye went on to loss of vision which decreased to finger counting at 4 meters. The first case (case 33) was not considered because a diagnosis of retinal detachment in the primarily affected eye had been made and treatment had been given. Fuchs summarized all 3 of his cases by saying that without a pathologic study the diagnoses would not have been made, and he stressed the importance of complete pathologic studies. He also mentioned 2 cases of metastatic melanosarcoma observed by him that fell into this group, but no pathologic evidence or description was given.

Meller [6] reported the case of a 28 year old man who had been blind in his left eye since the age of 21. For the past several weeks there had been inflammation of the right eye with conjunctival and ciliary injection and swelling of the iris. The left eye was enucleated; examination revealed sarcoma. Meller gave a detailed report of the patient's recent condition and of the histologic observations. There were no signs of syphilis or of articular rheumatism. There was no history of trauma.

Schwartz [13] reported the case of a man aged 38 who consulted him for inflammation and increased tension in his right eye. Under the influence of miotics the tension became normal, but symptoms of sympathetic ophthalmia developed in the left eye. The right eye was enucleated; it contained a sarcoma of the choroid. Tonsillectomy and drainage of the nasal sinuses were followed by rapid recovery. The conditions found in the enucleated eye are reported in detail. The tumor was almost entirely necrotic. The choroid presented diffuse proliferation of chromatophores, infiltrating lymphocytes, plasma cells and great numbers of epithelioid cells. Lesions were found in the eye, which had caused sympathetic ophthalmia. There was no history of injury.

Reis [7] reported the case of a 62 year old man who had a detachment of the retina in his left eye, followed later by severe pain and inflammation with marked elevation of tension. An anterior sclerotomy was performed on this eye. Sympathetic ophthalmia occurred in the right eye, and on enucleation of the left eye a diffuse sarcoma showing degeneration and necrosis was found. This case was discarded from our series because of the operative intervention.

Post [18] included in his review of sympathetic ophthalmia a case of definite necrotic sarcoma (case 3) in which the pathologic diagnosis was confirmed by Verhoeff. This is the case reported by Schwartz and included in our review.

REPORT OF A PERSONALLY OBSERVED CASE

On June 7, 1939, J. H., a 59 year old man, a native of Sweden, was admitted to the service of one of us (M. R.) at the Buffalo Eye and Ear Hospital, pleading to have his left eye enucleated immediately. He was having unbearable pain and was in a nervous and distraught state bordering on exhaustion. This was the culmination of weeks of severe pain and many sleepless nights. He stated that some time previously several ophthalmologists had advised enucleation of this eye but that he had procrastinated. He was positive that there had never been any injury to either eye.

A cursory examination revealed a totally blind, severely inflamed, staphylomatous left eye which appeared to be larger than normal. In the region of 6 o'clock there was a marked bulge of the iris and ciliary body. The pupillary area was filled with a grayish white mass which clinically resembled opaque lens structure. The anterior chamber was obliterated; the cornea was cloudy, and an anterior examination of the eye was impossible. A tentative diagnosis of absolute glaucoma with possible secondary endophthalmitis was made. The right eye showed slight circumcorneal injection, and the cornea looked a trifle cloudy. The visual acuity was 20/70. Pain was so extreme in the left eye, in spite of the hypodermic administration of ¼ grain (0.015 Gm.) of morphine sulfate, that the patient could not tolerate further examination. Because of this an emergency enucleation of the eye was performed. Local anesthesia was employed, the cone retrobulbar injection being supported by hypodermic injection of ½ grain (0.03 Gm.) of morphine sulfate. The operation was uneventful; no implant was used. The globe was sent to the Army Medical Museum for pathologic study and report. Within the next forty-eight hours the patient recovered completely from his pain and mentally was in a normal state, so that his right eye could be examined in detail and his history obtained.

History.—About three years prior to his admission to the hospital, vision became blurred and somewhat cloudy in his left eye. He consulted several ophthalmologists, who advised him that he had chorioretinitis in this eye and should be reexamined at periodic intervals. This advice was not followed until Dec. 1, 1938. At this time he was visiting relatives in Sweden and having periodic attacks of pain in his left eye, with marked failure of vision. He visited an ophthalmologist there, who advised immediate enucleation of his left eye. He refused this and returned to America. About April 1, 1939, his right eye became cloudy and he discovered that he could not see to read or write even with the aid of glasses. Pain was very severe in his left eye, but there was no pain in his right eye. Sedatives failed to relieve him, and even though several ophthalmologists advised enucleation of the left eye he continued to refuse operation. At no time was there any injury to either eye. The only general illness of any significance which he had ever had was chronic bronchial asthma for the past six years.

18. Post, L.: Sympathetic Ophthalmia, South. M. J. **27**:421, 1934.

Family History.—The family history was irrelevant.

Physical Examination.—The patient was well nourished and well developed. The ears, nose and mouth were normal. There were no palpable nodes in the neck, axillas or groins. The heart and lungs were normal. The abdomen showed no scars, tenderness or masses. The liver and spleen were not enlarged. Rectal examination and examination of the gastrointestinal tract revealed no abnormality. The extremities and the reflexes were normal. The Wassermann and Kahn reactions were negative. A roentgenogram of the chest showed thickening of both pulmonary hili, with some calcification in each. Linear markings were accentuated on both sides and extended well out to the periphery. There were no pulmonary metastases.

Ocular Examination.—Externally the right eye, except for a mild circumcorneal blush, looked quite normal. The pupil reacted sluggishly to light and in accommodation; motion in all directions was normal. Examination with the slit lamp revealed many deposits scattered throughout the endothelium of the cornea. The anterior chamber had an aqueous beam, with many cells. The iris was atrophic in appearance, with marked destruction of the margin. Many new blood vessels were present in the iris. There were many adhesions to the antreior part of the lens capsule, and the capsule was covered with brown pigment and deposits. The vitreous and the fundus could not be visualized because of the pathologic changes in the anterior segment. The vision in this eye was 20/70 and the tension was 17 mm. of mercury (Schiötz)—certainly a definite picture of chronic iridocyclitis.

Impression.—In view of the aforementioned findings a clinical diagnosis of sympathetic ophthalmia was made. This condition must have been present, according to the history, for at least two months.

Immediate Progress.—Atropine sulfate and hot packs three times a day were applied locally. Salicylates were given in fairly large doses orally, and a course of nonspecific protein injections was given parenterally. The left socket healed promptly by primary intention, and on June 13 the patient was discharged from the hospital. He was ambulatory. There was no improvement in his right eye. On June 19 a letter was sent to the Army Medical Museum concerning the clinical findings and the patient's progress. On June 21 the following report was received (E. De C.): "Preliminary histologic examination reveals the presence of a malignant melanoma of the choroid that has extended as a massive tumor into the vitreous chamber. There is also chronic uveitis somewhat suggestive of sympathetic uveitis. Have there been any suggestive clinical symptoms in the remaining right eye?" Our letters had just crossed in the mail and it is obvious that the pathologic diagnosis of sympathetic ophthalmia was made independent of the clinical report. The report of a malignant melanoma indicated the cause of the condition, which up to this time had been undetermined. In view of this finding the patient was referred to the State Institute for Malignant Disease for high voltage roentgen treatments to the orbit and complete physical examination. Because of the patient's long delay in having the enucleation performed it was deemed advisable to give the roentgen treatments even though the tumor was radioresistant.[19] Physical and roentgen examinations failed to reveal any metastases or involvement elsewhere in the body.

Further Progress.—There was a gradual loss of vision in the remaining eye, associated with marked increase of cells and pigment in the anterior chamber.

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19. Samuels, B.: Sympathetic Scleritis, Arch. Ophth. **10**:197 (Aug.) 1933.

Many precipitates, especially of the pellucid type, formed on the cornea. The pupil responded to atropine and was fairly dilated, but posterior synechiae continued to form. He was given a series of intravenous injections of typhoid H. antigen. This was followed by a complete course of uveal pigment desensitization as outlined by Woods [20] and by Woods and Little.[21] Interesting in this connection is the fact that in spite of definite corroborative pathologic evidence of sympathetic ophthalmia the uveal pigment cutaneous test was reported both by Dr. J. S. Friedenwald and by Dr. Allan Woods as giving a nonspecific reaction. In spite of all this treatment the vision decreased to 20/200. On October 17 the patient was hospitalized in the Buffalo General Hospital, and sulfanilamide therapy was tried at the suggestion of Dr. Sanford Gifford.[22] The treatment was carried on for one week, 120 grains (7.76 Gm.) the first day, 90 grains (5.4 Gm.) the second day and 30 grains (1.94 Gm.) daily for the rest of the week, with maintenance of a sulfanilamide concentration of 12 mg. per hundred cubic centimeters of blood. There was no improvement from this therapy. Solution of potassium arsenite U. S. P. and vitamin B_1 were given, in addition to a high caloric diet and general supportive measures. The vision continued to decline, and on December 7 it fell to finger counting at 4 feet (120 cm.). In view of this it was decided to employ Verhoeff's diphtheria antitoxin treatment.[23] Dr. Victor Cohen, an allergist, was consulted and took charge of the serum treatment. On December 7, 8, 11 and 12 diphtheria antitoxin (20,000 units) was given. On December 16 hives developed over the body and lips, associated with stiffness in the joints. Because of these symptoms this therapy was discontinued. The eye was much better until Jan. 4, 1940, when it became worse again. It was felt that the nonspecific effects of an allergic reaction were responsible for the original improvement; no further antitoxin treatment was given, and intravenous streptococcus vaccine therapy (National Drug Company, 2,000,000,000 organisms per cubic centimeter) was decided on. A series of injections was given, starting with 0.1 cc. and increasing to 0.4 cc. over a two month period. On March 1 the patient reported that after the last injection he had broken out with papular urticaria associated with much itching. The therapy was discontinued. On April 2 he reported that for the past two weeks he had had severe asthma. Examination of the chest showed it to be emphysematous; there were sibilant and sonorous rales. The heart showed a good tone; it was not enlarged, and there were no murmurs. Concentrated extract tests for allergy gave positive results for dust and feathers; he was given treatment for his allergic condition in graduated doses, with resultant improvement in the symptoms.

Since the diphtheria, streptococcus and extract therapy there has been a progressive improvement in the eye. On May 14 the vision was 20/70. No aqueous beam was present, and there were no active precipitates. The eye looked quiet and much clearer. Locally the following preparation was used: atropine sulfate, 0.05 Gm.; ethylmorphine hydrochloride, 0.25 Gm., and mercury oxycyanide solution (1:5,000), 10.0 cc., the ethylmorphine hydrochloride content being gradually increased. The fundus was visualized; it was grossly normal.

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20. Woods, A. C.: Sympathetic Ophthalmia: The Use of Uveal Pigment in Diagnoses and Treatment, Tr. Ophth. Soc. U. Kingdom **45**:208, 1925.

21. Woods, A. C., and Little, M. F.: Uveal Pigment Hypersensitivity and Therapeusis, Arch. Ophth. **9**:200 (Feb.) 1933.

22. Gifford, S.: Personal communication to the author.

23. Verhoeff, F. H., and Irvine, S. R.: Sympathetic Uveitis: Results of Treatment with Diphtheria Antitoxin in Twenty-Five Consecutive Cases, New York State J. Med. **36**:63, 1936.

At the time of writing (December 2) the crystalline lens is becoming cataractous, and because of this the vision is reduced to 20/100. Eventually operation will be required.

Pathologic Picture.—Gross Specimen: There was a firm bulb 24 by 24 by 24 mm. A slight bulging was present at 6 o'clock. The cornea was hazy and the

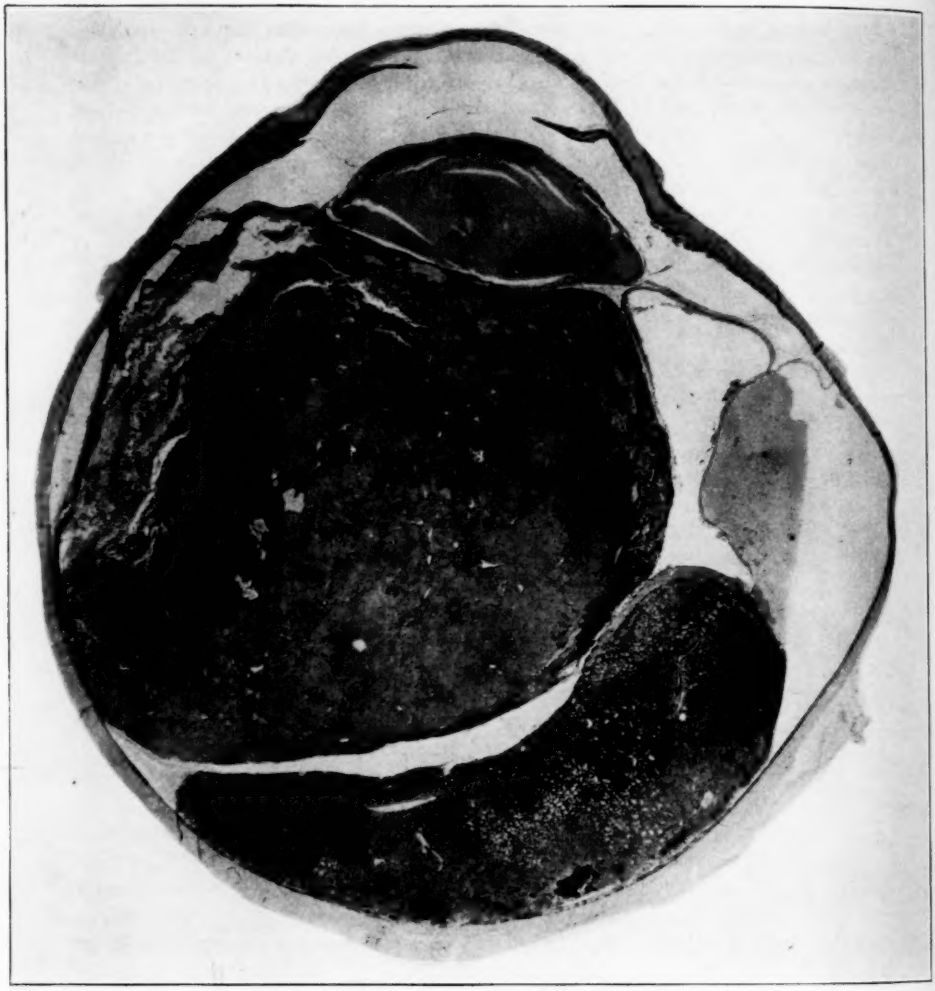

Fig. 1.—Microscopic section of the bulb. Hematoxylin and eosin, × 8. (Army Medical Museum negative 68797.)

bulb irregular. The eye was opened in the horizontal plane; it was filled with a dark brown friable mass. The lens filled the anterior chamber. The optic nerve was short. There was no visible perforation.

Microscopic Slide: Examination with the naked eye revealed an irregularly pigmented tumor mass occupying most of the vitreous chamber and pressing on the posterior surface of the lens. The iris and the lens were displaced anteriorly.

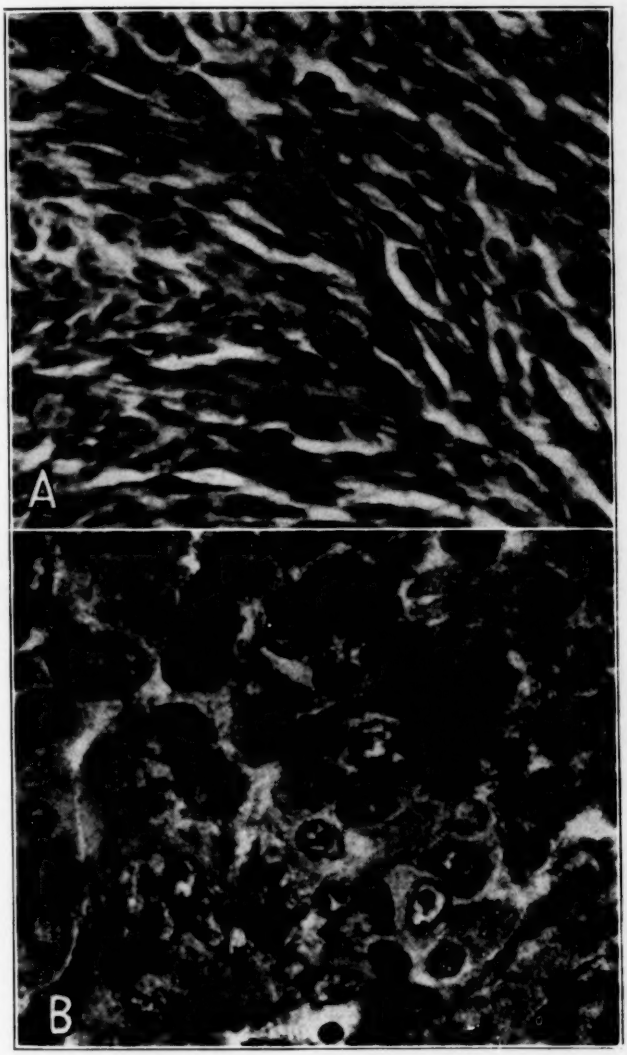

Fig. 2.—*A*, spindle subtype B cells. Hematoxylin and eosin; × 425. (Army Medical Museum negative 68802.) *B*, melanoma with epithelioid type cells. There is more pigment than is observed in spindle cells. Hematoxylin and eosin; × 915. (Army Medical Museum negative 68799.)

Low power magnification showed a tremendous choroidal tumor that had pushed the retinal remnants to the opposite side of the eye. The greater part of the retina was destroyed, either by infiltration or by compression degeneration. The tumor

mass had involved only a small part of the choroid, the greatest amount of growth being internal. The choroid was diffusely thickened, however, by round cell infiltration in which there were pale foci suggesting epithelioid cells. Near the ora serrata a discernible portion of retina was separated by a serous exudate containing vacuolated and pigment-laden large mononuclear cells. There were atrophy and distortion of the ciliary processes. Wide peripheral anterior synechiae and marginal posterior synechiae were present. A thin, fibrous, pigmented pupillary membrane was adherent to the lens. In the root of the iris there was an infiltration of plasma cells, lymphocytes, occasional granulocytes and numerous heavily pigmented large nononuclear cells. A slight diffuse infiltration appeared throughout the iris, but histologic sympathetic nodules were not seen. Large cells filled with melanin pigment lined the anterior surface of the iris and on one side filled the spaces (of Fontana) between the trabeculae of the filtration meshwork. Chronic inflammatory cells extended through the corneoscleral junction into the episcleral connective tissue, mostly in the perivascular areas. Albuminous fluid appeared in the anterior chamber. The periphery of the cornea presented slight vascularization and a few chronic inflammatory cells extending into the substantia propria from the episcleral dense round cell infiltration. A few leukocytes had infiltrated the conjunctival epithelium. Elastic fiber proliferation and granular degeneration were present in the limbic stroma. There was slight intracellular edema of the anterior corneal epithelium, with an increased number of infiltrating leukocytes. Bowman's membrane was thick. Descemet's membrane was somewhat thickened peripherally. The mesothelial cells lining the cornea presented adherent large mononuclear cells and occasional polymorphonuclear leukocytes. Occasional large and small "drusen" appeared on Bruch's membrane. The optic nerve head showed backward bowing of the lamina cribrosa, which, together with the arachnoid sheath of the nerve, was infiltrated with pigment-filled macrophages, some of which were difficult to distinguish from melanoma cells. A few discrete pigmented cells had infiltrated the optic nerve. The lens was adherent posteriorly to the necrotic retina, which was infiltrated with numerous pigmented mononuclears and with some leukocytes. In the lens substance there were foci where the layers were broken and separated by morgagnian globules of various sizes.

The tumor itself was greatly varied in pigmentation and was cellular. Large blood spaces were not a feature. Anteriorly there was some necrosis but very little round cell infiltration. There were two types of tumor cells, the most abundant being spindle-shaped cells whose nuclear chromatin was scant and generally condensed into a prominent nucleolus. These cells were very finely or not at all pigmented and were arranged in ill defined strands with scant fibrous tissue. In another large area, with a number of blood spaces apparently lined by tumor, the cells were large, each presenting an abundance of cytoplasm and a vesicular nucleus with a large, prominent nucleolus. These cells respectively, according to Callender's classification, were spindle cell, subtype B, and of melanoma cells of the epithelioid type. As shown by the Wilder reticulum stain, there were few argyrophil fibers in the tumor, which probably indicated high malignancy.

In the choroid, the vascular layer and the suprachoroidea were diffusely infiltrated with numerous round cells. Anteriorly this infiltration was less dense. In the posterior segment focal accumulations of epithelioid cells appeared. The centers of these foci were composed of typical epithelioid cells with an abundance of cytoplasm indistinctly delimited. An occasional leukocyte, lymphocyte or

eosinophil was observed among the epithelioid cells. A rare multinucleated giant cell was present. No central necrosis or caseation was seen. The zone around each focus was composed of lymphocytes. The distinctive feature of the epithelioid cells within the foci was that they contained melanin pigment within their

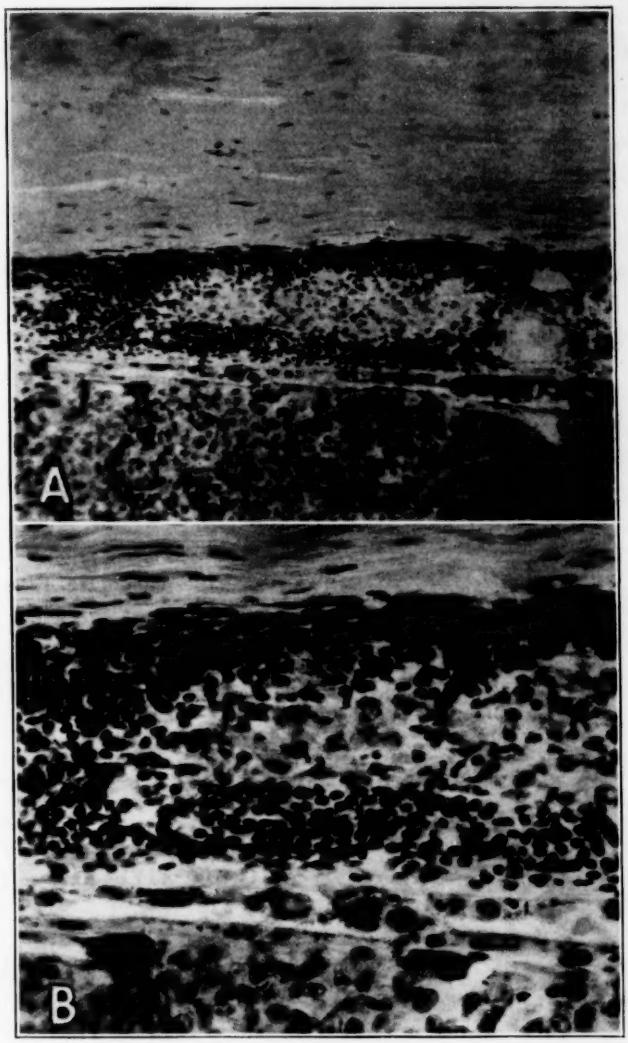

Fig. 3.—*A*, granulomatous nodule of sympathetic ophthalmia. Note the pale epithelioid cell focus surrounded by round cells in the choroid. The melanoma (at bottom) extends from elsewhere, the retina having been pushed away. The sclera appeared at the top. × 150. (Fort Sam Houston Hospital negative P3840.) *B*, high power magnification of *A*. Note the melanin pigment granules in the epithelioid cells of the granulomatous nodule. Pigmented melanoma cells are seen below. × 450. (Fort Sam Houston Hospital negative P38B40.)

cytoplasm. Indeed, they were the histologically typical nodules [24] of sympathetic ophthalmia. The same type of cellular infiltration extended into the sclera around the posterior ciliary nerves, except that epithelioid foci were absent.

Diagnosis.—The diagnosis was malignant melanoma of the choroid, mixed epithelioid cell and spindle cell subtype B, with invasion of the retina and the vitreous; secondary absolute glaucoma; sympathetic ophthalmia; cataract secondary to tumor growth, and detachment of the retina.

CONCLUSIONS

Sympathetic ophthalmia due to sarcoma can and does occur without injury or perforation of an eye. After a careful perusal and study of the literature it is with a reasonable degree of certainty that we conclude that to date there are 5 authentic cases on record, 3 reported on the Continent and 2 (including our own) in the United States.

A careful pathologic study of every bulb enucleated is a valuable adjunct to clinical studies, which must include slit lamp microscopic examination. Clinical interpretations are much more accurate and important when the basic histologic and pathologic picture is thoroughly interpreted and understood.

Any explanation of the exact cause responsible for sympathetic ophthalmia in this series of cases would be purely theoretic and not within the scope or purpose of our paper.

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24. DeCoursey, E., and Ash, J. E.: Atlas of Ophthalmic Pathology, ed. 2, Omaha, American Academy of Ophthalmology and Otolaryngology, 1939, p. 74.

PRACTICAL APPLICATIONS OF DYNAMIC RETINOSCOPY

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Dynamic retinoscopy is a system of retinoscopic examination in which the eyes are made to engage actively, accommodating and converging during the test. It is therefore in a sense the very opposite of ordinary, or static, retinoscopic study, in which the eyes, specifically the neuromuscular mechanism of the eyes, are made to relax as completely as possible, with or without cycloplegia. There are a number of more or less useful applications of dynamic retinoscopic examination. I shall touch briefly on a few.

Dynamic retinoscopic examination can be used to determine whether or not a seeing eye, whatever its degree of vision, has any accommodative power. And, if it has, it will show approximately how much it has. In a general study of accommodative activity it acts as an objective pathfinder and as a check on the subjective methods. A check is desirable, as these methods have some deficiencies. For example, the usual subjective method for finding the amplitude of accommodation is locating the near point of accommodation. Now there is no correlation between the size of type used, in terms of the visual angle, and the position of the near point. For instance, if the nearest point the patient can see the smallest type of the reading chart is, say, 5 inches (12 cm.) one says that he has 5 D. of accommodation. One does not know, however, whether his eyes are really in focus at 5 inches, as the visual angle subtended by the type seen at that distance is usually larger than the minimum; it may be, in fact, twice the minimum visual angle for that particular patient. In cases of normal distant vision and with the smallest type on the Jaeger chart this deficiency is not important. But in cases of subnormal vision (amblyopia of one or both eyes) the lack of correlation between the size of type used and the position of the subjective near point is important. Secondly, it is not possible in the subjective test to individualize the accommodative power of each eye while the eyes are engaged binocularly. The patient cannot analyze his visual sensations so as to know whether what he sees is seen with both eyes or with one eye and, if with one eye, with which. Both of these deficiencies, especially the latter, are overcome by the objective tests.

Presented before the New York Society for Clinical Ophthalmology, Dec. 2, 1940.

The method is to have the patient, with his distance correction on, fix binocularly a target held by the examiner a little in front of the retinoscope. The examiner can start at arm's length, about 26 inches (66 cm.), and hold in front of the retinoscope a simple target, such as a white-headed pin; or the target may be the examiner's finger or, preferably, the patient's finger held by the examiner. The examiner instructs the patient to look closely at the target while he flashes the light across both eyes and watches the reflex. There may be a "with" movement in each eye at the start, especially if the target is held very close to the retinoscope. The examiner then, concentrating his attention more on one eye at a time while both eyes fix the target, moves the target toward the patient until he gets an "against" movement. He then proceeds to move in closer to the patient, always keeping the target some distance in front of the instrument, until the "against" movement stops. The examiner's position at that point, which may be measured or left to judgment, is practically the near point of accommodation found objectively.

The test can be refined by the use of various targets and by working along a measured rod or tape, but reduced to its simplest fundamentals it can be made in this way. The location of the near point can be judged by the examiner. Here the accommodation of each eye is measured while both eyes are engaged in seeing or trying to see. Moreover, no matter how poor the distant vision of an eye, if there is any accommodative power in that eye it will show up, especially if the patient's own finger is used as a target.

A corollary use of this method is to determine the depth of cycloplegia by finding how much residual accommodation is left in each eye. This knowledge has some bearing on the postcycloplegic tests. It is very difficult to measure this residual accommodation subjectively, for the reasons previously mentioned, in addition to which there is the great handicap of a dilated pupil. For example, if a 4 mm. pupil is dilated to only 6 mm. the area is enlarged about two and one-half times, and the amount of light entering the eye through the ring of pupil around the central 4 mm. zone is about one and one-half times as much as enters through the normal 4 mm. pupil. The patient's vision is the result of this whole volume of light—central and peripheral—and the state of his vision is affected by all the aberrations incident to a dilated pupil. Subjectively there is no way of separating the centrally entering light from the peripherally entering light. Objectively the examiner can watch the behavior of the central reflex and ignore the periphery, thereby getting more nearly the refraction of the normal optical zone.

The test can be made by the examiner working as previously outlined, keeping his distance at arm's length and holding the target in

front. Working from eye to eye, an "against" movement indicates that there is a residual accommodation of 2.00 D. or more. A "with" movement, even when the target is moved close to the patient, indicates a residual accommodation of less than 2.00 D. By inserting a + 1.00 D. lens before each eye or by working at a further range the limits of the residual accommodation can be set to be either above or below 1.00 D. By working from one eye to the other a comparison of the depth of cycloplegia in the two eyes can also be made at the same time.

Another use of dynamic retinoscopic examination is to compare the accommodation of the two eyes as to quantity and quality, that is, to determine whether the two eyes can accommodate to the same extent and with equal facility. Facility implies power of sustained accommodation and rapidity of accommodative adjustment from one distance to another.

The test in the simplest form can be made in the way previously outlined. The examiner, at arm's length, holding the target very close to him, flashes the light rapidly across first one eye and then the other. This will generally produce a "with" movement in both eyes. He then moves the target toward the patient, "scoping" the eyes alternately, until he gets an "against" movement in both eyes. If the "against" movement appears in one eye before it does in the other, the latter eye has less accommodation. This may be due to this eye actually having a measurable amount less accommodation, or, more likely, this eye may be slightly undercorrected with plus or overcorrected with minus. A check on the distance correction is the first thing indicated. This can be done after adding a plus to the lagging eye to equalize the position of the "against" movement in the two eyes. If this change is not accepted at distance it indicates a measurable amount of unequal accommodation. Inequality in efficiency of accommodation will show itself by a lag in adjustment and sustained action in one eye as compared to the other. This will show objectively by an unstable reflex movement in one eye as compared to a definite sustained "against" movement in the other eye.

Another application of dynamic retinoscopic examination is to check for overcorrection in cases of myopia and also for probable strain at near vision from a full correction. The test is based on the following observation. If a young emmetrope with ample accommodation is made to fixate a target in the plane of the retinoscope at 14 or 15 inches (35 to 38 cm.) and the eyes are examined retinoscopically, a "with" movement will be obtained. It will take an addition of + 1.00 to + 1.50 D. before each eye to cause a reversal, that is, not just a neutral or indefinite movement, but a distinct "against" movement. In applying the test in the presence of myopia in a young person, the patient, with his distance

correction on, is asked to fixate the letters or figures on the retinoscope held about 14 or 15 inches away. If there are no fixation marks on the retinoscope the patient may be asked to fix intently with both eyes the examiner's brow. The initial "with" movement is observed, and a + 1.00 D. sphere is applied to each eye. A convenient way of applying these lenses is to have them mounted in a light-weight front such as this and held up by the examiner's free hand in front of the patient's distance correction. A few lenses mounted in this way are convenient for various dynamic tests. If there is now an "against" movement, the distance correction is, if anything, a slight undercorrection, and no further work is necessary. If, however, the addition of + 1.00 D. before each eye still gives a "with" or neutral movement, the test is continued and + 1.50 spheres are interposed before each eye. If this gives an "against" movement, the distance correction may be considered a full correction and not likely to cause any discomfort. But if the + 1.50 spheres do not give the expected "against" movement, then either the distance correction is an overcorrection, or even if not, the lenses will most likely prove uncomfortable for near work. The remedy is either to reduce the distance correction or to give a plus reading addition.

Of course, the several tests just mentioned, except for checking the depth of cycloplegia, must be made while the eyes can use their full accommodative power. They must therefore be made as precycloplegic or postcycloplegic tests when cycloplegia is used.

A final word: The objective tests just mentioned differ from the usual subjective tests in several respects, but one important difference is that they can be made while the eyes are engaged in natural binocular vision. In subjective testing it is not possible to study the behavior of each eye during the act of seeing with both eyes except, to a limited extent, by introducing artificial devices, such as stereoscopes or red and green spectacles. But objectively the eyes can be individualized, and the behavior of each eye can be studied while both eyes are engaged in the act of seeing. This to me seems significant, because I believe that the act of seeing with both eyes is an entity *sui generis;* it is a distinctive physiologic activity and not merely a blending of the acts of seeing with each eye alone. To use perhaps a crude analogy, the act of walking is a coordinated activity of the two feet, but this combined activity is certainly not a blend of the individual acts of hopping on each foot alone. I believe that the more the tests conform to the normal way of binocular vision, the better the results will be. The dynamic tests mentioned, since they enable the examiner to study each eye while both eyes are engaged in the act of seeing, have therefore some unique and distinctive features.

Clinical Notes

BLOOD STAINING OF THE CORNEA

Report of a Case

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Complete blood staining of the cornea presents a characteristic picture. When bleeding into the anterior chamber occurs and a hyphema forms, corneal staining may become evident in a few days, especially in conditions accompanied by increased intraocular pressure. The condition is always the result of an injury or wound and is a pathologic rarity. According to Duke-Elder,[1] its rarity is explained by the fact that the intraocular tension is lowered in most instances of perforating injury. The coloring of the cornea varies from a rusty brown to a greenish black or from greenish yellow to white. The cornea may, in the beginning, be entirely stained and clears very slowly. Schousboë and Morard [2] stated that its appearance may be limited to a discoid stain in the center area only. When clearing occurs it starts peripherally and travels centrally. A gray central patch may persist after a year, and it may take more than two years for it to clear completely.

The case reported here specifically demonstrates the influence which increased intraocular tension bears on this condition. It also shows the same sequence of clinical events as reported in typical cases [3] in the past.

Read before the Brooklyn Ophthalmological Society on Feb. 20, 1941.

1. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 2038.

2. Schousboë, F., and Morard, G.: Infiltration hématique disciforme de la cornée, Bull. Soc. d'opht. de Paris, 1935, pp. 17-21.

3. (*a*) Gradle, H. S.: Bilateral Blood Staining of the Cornea, Illinois M. J. **42**:281-285, 1922. (*b*) Collins, E. T.: Discoloration of the Cornea with Blood Pigment, Tr. Ophth. Soc. U. Kingdom **15**:69, 1895. Maghy, C.: Blood Staining of the Cornea, California & West. Med. **24**:637-639, 1926. Morgan, O. G.: Blood Stain of Cornea, Proc. Roy. Soc. Med. (Sect. Ophth.) **22**:10, 1928. De Courcy, T. L.: Case of Blood Staining of the Cornea, Tr. Ophth. Soc. U. Kingdom **53**:597, 1933. Maghy, C.: Observations of Blood Staining of the Cornea, Am. J. Ophth. **2**:633-636, 1919. Ball, J. M.: Discoloration of Cornea with Blood Pigment, Tr. Ophth. Div. Am. Acad. Ophth., 1903, p. 181; Am. J. Ophth. **20**:364-366, 1903. de Schweinitz, G. E.: Absorption of the Blood Pigment After Staining of the Cornea, Ophth. Rec. **6**:631, 1897. Lawford, J. B.: Coloring Matter Blood Pigment in Cornea, Tr. Ophth. Soc. U. Kingdom **8**:60, 1887-1888; **14**:74, 1893-1894. Griffith, J.: Blood Staining of Cornea, Tr. Ophth. Soc. U. Kingdom **14**:74-76, 1893-1894; **15**:86, 1895. Collins, E. T.: Two Cases of Staining of Cornea by Blood Pigment, ibid. **11**:43-47, 1890-1891. Weeks, J. E.: Peculiar Pigmentation of the Cornea, New York Eye & Ear Infirm. Rep. **1**:37-43, 1893.

REPORT OF CASE

I. D., a white woman of 61 years, was enrolled in the clinic of Dr. Walter V. Moore at the Brooklyn Eye and Ear Hospital on Sept. 23, 1935. She had bilateral immature cortical cataracts. Ocular and medical surveys gave negative results. Both preliminary iridectomy and extraction of the cataract in the left eye were accompanied by hyphema, which was absorbed readily without complications. Tension at all times was normal in this eye.

A preliminary iridectomy in the right eye on Nov. 28, 1939 was followed by hyphema and a rise in tension to 41 mm. (Schiötz). Three days after operation the chamber was full of blood and gave a "steel ball bearing" appearance. The gross picture was that of an anteriorly dislocated lens. One week after operation a deep, reddish brown staining of the posterior half of the cornea was seen. By the tenth day this pigmentation had extended peripherally almost to the limbus and anteriorly to Bowman's membrane. The picture remained the same till the thirty-third day, when a rather sudden change occurred. The staining became a light greenish gray. The cornea cleared slightly in the periphery, and in this area a few bright sharp green spots could be seen microscopically. The tension became normal for the first time since the operation and remained so afterward.

One year after operation the stain was dark yellow and occupied a round central area of cornea, 6 mm. in diameter. In the pigmented district the entire thickness of the stroma was involved. The remaining 3 mm. peripheral strip of cornea was clear on slit lamp examination except for a few widely scattered bright, sharp yellow granules in the stroma. These were the size of pinpoints under low power magnification. As much of the chamber and iris as could be seen was clear.

When the patient was last seen, Feb. 15, 1941, fifteen months after the operation, the right eye showed a light yellow horizontal cigar-shaped band of stain, 5 by 2 mm., in the center of the cornea. This was located in the middle of the stroma. The remaining cornea was clear except for the same yellow pinpoint-sized dots previously observed.

COMMENT

This case is presented not only because of the infrequent occurrence of corneal staining but also for a consideration of those facts in the case which might help in the management of the condition in future cases.

The possibility of making a diagnosis of anteriorly dislocated lens exists. Wadsworth [4] reported a case in which the picture so simulated such a condition that an operation was attempted. Careful slit lamp examination and a search for details of the lens should eliminate this difficulty. The duration of the staining in a particular case might tempt one to offer a poor prognosis. Corneal hematogenous pigmentation does clear, although it takes some time. It will be interesting to note what happens to this patient at any future operation. She still has her cataractous lens. The patient reported on by Gradle [3a] had further operations without resultant corneal staining, and he suggested that one staining might have immunizing power.

The relation increased intraocular tension bears to this condition cannot be overlooked. This patient had two operations on her left eye.

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4. Wadsworth, O. F.: A Case of Discoloration of the Cornea by Blood Pigment, and One of Hemorrhage into the Cornea: Pathological Examination by F. H. Verhoeff, Tr. Am. Ophth. Soc. **10**:594-604, 1903-1905.

Both were accompanied by hyphema, yet in neither did corneal staining occur. There was no increased tension in this eye. In the right eye, however, where there was increased tension, typical blood staining occurred. Furthermore, more rapid clearing in this and in other reported cases occurred only after the tension had gone down. A patient who shows bleeding at one intraocular operation should be carefully investigated as to the condition of the blood. Local and general measures should then be instituted in order to prevent a recurrence at a future intraocular operation, particularly in cases in which increased tension enters in any part of the picture.

PREVENTION AND HANDLING OF COMPLICATIONS ARISING DURING AND AFTER CATARACT EXTRACTION

SOME PRACTICAL POINTS

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The removal of senile cataract may be attended by unexpected complications as well as by complications which have been foreseen in the individual case. The surgeon will do well to anticipate if possible all the exigencies which may arise for each patient so that he may be prepared to apply the proper treatment. For any one to state that he has encountered no complications and expects none during or after this operation is pure folly. The wise operator will recognize the fact that difficulties do arise and that they come to the best surgeon. He will do all he can by study and by analysis of the experience of others and of his own experience to broaden his knowledge and to increase his armamentarium in the prevention and handling of complications as they arise. I shall review in detail in a practical way the methods which I have been in the habit of applying in cases of cataract requiring surgical intervention. Many of the points to be discussed have been learned from others. Their sources may be easily discovered. Other points are either original or in such general use that their application is common knowledge. For the latter no especial reference is required. For the first class a reference will be given only when it will add to the value of the paper. It is not necessary to review statistics prior to the excellent paper of Berens and Bogart.[1]

The experienced surgeon should be confident of his ability to carry a cataract extraction through to successful, uneventful completion or to a satisfactory conclusion as determined by the complications which are

This material was used in the course of instruction of the American Academy of Ophthalmology and Oto-Laryngology, Cleveland, October 1940.

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1. Berens, C., and Bogart, D.: Certain Postoperative Complications of Cataract Operations, Tr. Sect. Ophth., A. M. A., 1938, pp. 238-283.

present or which arise. He should by his demeanor and by his voice transmit this confidence to the patient. He should be calm and unruffled in his behavior even in the face of difficulties. He should be unhurried in the conduct of the operation. He should find no need for working against time or for believing that the sooner the operation is over the better. He should allow sufficient time for the anesthetic to take effect, for blood to clot and for observation of the effect of what he has done before he proceeds with the next step.

THE MOST IMPORTANT COMPLICATIONS

The most important complications of operation for cataract are (1) local complications, such as hemorrhage, loss of vitreous, prolapse of the iris, failure of apposition and healing of the wound, corneal opacity, infection, inflammation and glaucoma, and (2) general complications, such as drug reactions, delirium, retention of urine and respiratory, gastrointestinal, vascular and cardiac disorders.

GENERAL COMPLICATIONS

The general complications may be briefly considered first.

Respiratory Conditions.—A recent acute infection of the respiratory tract is a direct contraindication to operation. Asthma, hay fever, chronic bronchitis or any other source of coughing, etc., is not a direct contraindication to operation but should be handled in such a way that it will interfere as little as possible.

Drug Sensitivities.—Drug sensitivities may well be determined before the operation. Particularly should use of opium and its derivatives be avoided or reduced to a minimum, because of the dangers of nausea and vomiting. A trial of the various drugs which one anticipates using should be conducted before the operation. An inquiry into the drug history of the patient may give useful information. The patient may be given the various drugs on different days before the operation so that their effects may be noted. The postoperative conditions cannot be duplicated, but the reactions will be indicative. It is hardly necessary to perform patch tests for sensitivity to drugs used by instillation.

Delirium; Disorientation; Psychoses.—Seldom will a history of psychosis be elicited from the average patient with cataract. With institutional patients, of course, the facts are known in advance. Delirium, disorientation, hallucinations and delusions may develop in any elderly patient with cerebral arteriosclerosis after operation, the particular precipitating factors being (*a*) the bandage or mask covering both eyes and (*b*) the use of drugs. If and when such a disorder develops, the untreated eye should be opened and, if necessary, the patient allowed out of bed while attempts are made to restore sanity.

Fortunately the mental aberrations usually subside rapidly, and the eyes (if the wounds are sutured) suffer no damage. In fact, it is notorious that they do well. This experience gives one greater assurance in allowing considerable liberty to the average patient with cataract, the period of enforced rigid rest being shortened and the rules regarding raising the head and turning the patient made less stringent. In general, it has been learned that it is worth while to keep the patient relaxed and comfortable.

Retention of Urine.—The retention of urine, particularly by the male patient, may be embarrassing and disturbing. A history of prostatic disturbance with retention requires a preoperative examination. If retention develops after operation for cataract, it is better to elevate the head of the patient and even to let him sit up or get out of bed after twenty-four or thirty-six hours to urinate rather than to subject him to further discomfort, medication or the dangers of catheterization.

Cardiorespiratory Disorders.—The danger of cardiac failure, embolism, thrombosis and other vascular disorders is not great after operation for cataract with local anesthesia. However, hypostatic pneumonia may and does occur in patients with weak circulation. The best treatment is preventive; there should be a short stay in bed, the patient being turned and allowed to get out of bed if there is any sign of pulmonary edema due to the continued recumbent position.

Hypertension.—If the blood pressure is increased at the time of the operation or shortly after, there is an added danger of complicating hemorrhage. If the systolic pressure is high and the diastolic pressure normal, often improvement in the condition may be obtained by sedatives and by preoperative rest in bed. A high diastolic pressure, however, gives a graver prognosis, because of the increased pressure in the uveal tract and because of the probability of existing organic vascular changes. When the intraocular pressures have been altered by the incision and by the escape of aqueous, the continued high diastolic pressure in the uveal tract may cause hemorrhage if the vessels are fragile, or it may without hemorrhage lead to increased bulk of the vascular bed and thus secondarily produce increased pressure on the vitreous.

Diabetes.—Lowered carbohydrate tolerance is frequent in the elderly. Restriction of starch and sugar intake is the natural thing for the average patient with cataract. Cataract is more frequent in the diabetic than in the nondiabetic patient but is not necessarily always caused by the disturbed carbohydrate metabolism in the particular person. The preparation of a diabetic person for surgical treatment of cataract involves getting him into the optimum condition for avoidance of hemorrhage and infection, which are more common in diabetic than in nondiabetic persons, and for promotion of healing, which is recognized as retarded

in diabetic persons. A prolonged period of study of the individual patient is necessary, with adjustments of diet and the use of insulin so that the patient will react to his best advantage. The optimum condition is not always present when the urine is free of sugar or when the level of sugar in the blood is the lowest. Rather, it must probably be judged by the level at which the sense of well-being is best maintained. Operation should be postponed until this level can be attained.

Gastrointestinal Conditions.—The gastrointestinal tract should have any needed attention before the operation. The dietary habits of the patient should be known, and if necessary a laxative should be administered sufficiently in advance of the operation. Many elderly persons eat more protein food than is necessary for their bodily requirements. It may be well to reduce the intake of meat, eggs, cheese and fish. It may be unwise to substitute foods to which the patient is unaccustomed. Excessive use of caffeine-containing beverages, drugs, alcohol and nicotine should not be permitted. On the other hand, their use in moderation may be comforting. It is best to bear in mind the need to make the patient comfortable, confident and relaxed. The usual plan is to keep the intestinal tract quiet for two or three days. There is no contraindication to movement of the bowels, but there should be no straining at stool or difficult manipulation of the bedpan. If necessary, it will be better to get the patient out of bed than to make him uncomfortable. Cascara given on the third night after the operation, followed by a mild saline laxative given by mouth or by an enema for those who prefer it, usually works well. The postoperative diet for the first four days should be such as to require no chewing. In the case of patients who are uncomfortable without their false teeth it seems best to permit the use of the dentures.

Syphilis.—If syphilis is discovered by history or by routine examination of the blood it is best to postpone the operation until the disease can be adequately treated.

Tuberculosis.—Active tuberculosis is a direct contraindication to surgical treatment of cataract, because of the possibility of untoward reaction to surgical trauma. The discovery of a positive Mantoux intradermal reaction to old tuberculin is not a contraindication.

Focal Infection.—This will be more thoroughly considered under the headings of infection and inflammation, but in general it may be said that focal infection interferes with the healing process. If the patient gives no clinical sign of inflammatory disease due to focal infection, such as arthritis, it may be unwise to interfere with the foci of infection. If teeth are removed or other foci are opened, sufficient time should elapse between this preliminary work and the ocular operation for the patient to recover completely.

LOCAL COMPLICATIONS

General Preventive Measures.—Measures designed to improve the morale of the patient and his confidence in the surgeon are very important. Careful preparation [2] of the patient will help to prevent complications. Laboratory, clinical and other examinations should be made to exclude syphilis and other diseases which will predispose to infection, inflammation, hemorrhage or thrombosis. The use of vitamins may help in the prevention of hemorrhage and in the promotion of healing. Local antiseptics have not been found of much value in protecting from infection patients in whose cases pathogenic organisms are obtained by culture of material from the skin, lid margins and conjunctivas. Patients in whose cases positive cultures are not obtained should not be subjected to the necrotizing, devitalizing and irritating effect of strong antiseptics, such as silver nitrate. One may better depend on the immunity of the patient unhampered by the use of such agents. Local anesthesia should be complete, and its induction (by injection of procaine hydrochloride) should be careful. In some instances the use of avertin with amylene hydrate per rectum may be advisable. Sedatives help greatly in producing general relaxation and freedom from annoying fear and tension. The advantages of retrobulbar block anesthesia and partial akinesia of the extrinsic ocular muscles far outweigh the occasional complication. The point of the needle in its advancement should be preceded by a drop of the anesthetic solution so that the vessels in the path of the needle will not be injured. Akinesia of the facial muscles obtained by O'Brien block of the upper branches of the seventh nerve or by the infiltration method is now almost a necessity. If procaine hydrochloride does not give satisfactory local anesthesia, as it does not in a small percentage of patients, injection of 2 per cent cocaine hydrochloride (0.5 cc.) may be made subconjunctivally or beneath Tenon's capsule. If cocaine or epinephrine is used, care must be exercised against untoward effects. If the limbus incision has been started or partially completed and the anesthesia is not sufficient the surgeon should stop and give more of the anesthetic. Pain leads to loss of control and coordination on the part of the patient and to unfortunate complications. The use of a good speculum or lid retractor and inspection to make sure that there is no pressure on the globe, particularly at the equatorial area, are important. If pressure is present it is necessary to do an external canthotomy and to make this sufficient to free the globe from pressure. Sutures which include the outer third of the scleral edges of the limbus incision rather than simply the conjunctiva bring into accurate apposition the lips of the incision and help greatly to reduce

2. Lancaster, W. B.: The Cataract Operation: A Study of Details, Surg., Gynec. & Obst. **52**:452-461 (Feb., no. 2A) 1931.

the dangers of hemorrhage, loss of vitreous and prolapse of the iris and to prevent downgrowth of epithelium into the anterior chamber. The sutures promote early reformation of the anterior chamber and proper healing of the wound with a minimum of astigmatic aberration. If the eyes are deep set this feature often does not cause difficulty unless there is absorption of fat almost to the cadaveric stage, so much so that the cornea is set near the level of the lateral orbital margin. Usually the conditions associated with deep-set eyes offer factors of safety. If there has been loss of lid tissue and if there is ectropion or lagophthalmos, it is advisable to repair the condition before operating for cataract. If this is not feasible, however, suturing the lids together after the cataract extraction is advisable. If exophthalmos exists because of increased orbital bulk, as in cases of disease of the thyroid, or because of neoplasm or inflammation which has been controlled, or if the eye is prominent as it is in some cases of high myopia, added precautions against loss of vitreous and exposure of the cornea must be taken.

Resistance to Infection and Inflammation.—In some cases vitality is manifestly low and healing power correspondingly reduced. In these general tonic measures may help, although in a few of them nothing seems to improve the condition. To patients with good constitutions but with evidence of focal infection—for example, the presence or history of infected teeth, infected tonsils, infected sinuses or colitis—it may be well to administer mild nonshock doses of nonspecific protein therapy after first testing for sensitivity to the agents employed. A convenient agent is typhoid vaccine. A test should be made with 0.1 cc. given intradermally. If a marked reaction occurs, great caution must be used. If no marked sensitivity is present, repeated subcutaneous doses, such as are used in typhoid immunization, may well be of value prior to operation. Shock reactions should be avoided.

Preoperative Examination of the Eye.—The preoperative ocular examination may disclose features which will indicate or predispose to complications during and after the operation. Chronic primary glaucoma, undetected and untreated, may prove a very serious complication of surgical removal of cataract. Chronic uveitis in any form, vascular disease and other intraocular disease, such as fluid vitreous, detachment of the retina or choroidal sarcoma, should be ruled out as far as possible by a complete examination, including tonometric studies, transillumination and slit lamp microscopic examination. If the presence of any important known complicated condition is ascertained, the surgeon will be prepared to act accordingly.

Glaucoma.—In general, the intraocular tension should be as nearly normal as possible before cataract extraction. In a case of unrecognized glaucoma the incision may gape and the corneal flap buckle after the

cataract section. If chronic primary glaucoma [3] is present, an iridectomy or a filtering operation should be done well in advance (at least six weeks before extraction of the cataract). At the time of the extraction the intraocular tension will guide the surgeon in his procedure. If the tension is still above normal a second attempt at reduction should be made. If the tension is normal the filtering area should be avoided and a corneal section made. If the tension is 8 mm. of mercury (Schiötz) or below the surgeon may make his section through the limbus and the filtering area in the hope that this may on healing raise the tension somewhat. Experience has shown that these procedures are of practical value. If the intraocular tension is elevated because of increased retrobulbar pressure, for example, by retrobulbar hemorrhage, appropriate measures for its relief must be undertaken before the eye can be safely opened by incision. Glaucoma caused by swelling of the lens in the intumescent stage of cortical cataract is rather rare but of sufficient importance to cause one to be on guard and not to allow patients to go through the process of maturation of cataract unwatched. Certainly the ocular tension in such circumstances should be estimated with the aid of the tonometer. The eyes from which such cataracts have been removed during the stage of increased intraocular tension have not done well. The results of removal of cataract which has caused glaucoma are not good. The glaucoma should be treated first and the cataract removed later.

Glaucoma Capsulare.—Glaucoma capsulare [4] is an interesting condition, depending, if the premise is correct, on the deposit in the angle of the anterior chamber of the small particles of the most superficial lamella of the anterior lens capsule which have flaked off in this peculiar degenerative process. I believe that the rise of intraocular tension is not caused by flakes blocking the angle as much as by the degenerative process also affecting the endothelial cells of the angle through which filtration takes place. However, it seems natural to assume that the flakes have much to do with the blockage and to recommend that the lens be removed within the capsule to remove the factor of exfoliation. I have used a filtering operation preceding or accompanying the extraction. The zonular fibers are fragile and degenerated in such cases, and the cataract may best be removed in the capsule.

Secondary Glaucoma.—Secondary glaucoma [5] following cataract extraction may arise from blockage of the angle and reduction of filtration

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3. Wheeler, J. M.: Cataract After Glaucoma: Its Etiology and Treatment, Tr. Am. Acad. Ophth. **28**:174-187, 1923.

4. Irvine, R.: Exfoliation of the Lens Capsule (Glaucoma Capsularis), Tr. Sect. Ophth., A. M. A., 1939, pp. 424-450. Kirby, D. B., in discussion on Irvine.

5. Weeks, J. E.: Glaucoma After Cataract Extraction, Tr. Am. Acad. Ophth. **28**:162-174, 1923.

by scar tissue, incarcerated iris, inflammatory tissue, pigment debris or deposits. The limbus incision if placed properly is just anterior to Schlemm's canal. Formation of scar tissue may render inefficient or destroy completely the drainage function of the angle throughout the length of the incision. Fortunately, nature usually provides for such emergencies, furnishing more than the area of drainage needed, and the remaining area is sufficient. It is a wise precaution at the end of an operation to make sure that the iris is not caught between the lips of the limbus incision before tying deep sutures which may so engage the iris that it is difficult if not impossible to free it with the spatula. The use of physostigmine in some form after intracapsular extraction is a great help in drawing the iris into the anterior chamber even when a complete iridectomy has been made. Atropine has been found to work best in cases of capsulotomy. Its common use may be an indication that a greater or lesser degree of iridocyclitis is expected after the extracapsular operation.

A rise in tension early in the healing process after cataract extraction is often well controlled by paracentesis, with repeated openings if necessary.

Delayed Postoperative Secondary Glaucoma.—With either an extracapsular or an intracapsular procedure, glaucoma developing late in healing or after healing is difficult to handle. Paracenteses in this stage are of no value. Trephining, sclerectoiridectomy, iridenclisis, iridotasis or any operation on the anterior segment is difficult and unsatisfactory. Perhaps the most satisfactory procedure is cyclodialysis with or without iridectomy. Occlusion of the pupil with iris bombé may respond to transfixion. Operations on the posterior segment are unsatisfactory and not without danger.

Epithelization of the Anterior Chamber.—The invasion of the anterior chamber by the downgrowth of epithelium may be prevented by prompt healing of the incision. Properly placed deep appositional sutures help very much. If the surface epithelium does invade the anterior chamber, as it may in gaping wounds or in corneal sections without conjunctival flaps, and a localized cyst is formed in a portion of the anterior chamber the cyst may be eradicated and its lining epithelium destroyed by aspiration [6] of the cystic contents and treatment with half strength tincture of iodine. The technic of this method, which has been shown to be effective and has been used by Knapp and others, is as follows: Local anesthesia, having been induced, the point of a sharp 27 gage needle attached to a small syringe containing 0.5 cc. of the iodine solution is inserted by boring rotation of the syringe through the cornea into the

6. Knapp, A.: Aspiration of Cyst of Anterior Chamber and Treatment with Iodine Solution, personal communication to the author.

cyst, the eye being held with a fixation forceps opposite the puncture point by an associate. The syringe is steadied, and the fluid content of the cyst is withdrawn, being mixed with the iodine solution in the syringe. Then the mixture is injected and again withdrawn. This procedure is repeated once more, care being taken not to distend the cyst wall too much. The fluid mixture is finally withdrawn, the cyst wall being left collapsed. Shrinkage usually occurs, and the cyst does not reform. Undue reaction may follow more trauma or escape of iodine solution into the anterior chamber. The same type of cyst and the more serious condition of complete epithelial lining of the anterior chamber may be treated with radium as Vail has suggested or with roentgen rays as reported by Perera. Filtration operations are of no avail. In the presence of generalized epithelization of the anterior chamber the prognosis is bad.

Hypotony.—Hypotony, or reduced intraocular pressure, as indicated by tension below 8 mm. of mercury (Schiötz), discovered before operation gives a poor prognosis, graded on the degree of hypotony. If the intraocular tension is too low to register with the tonometer (and particularly if such pressure is associated with increased protein in the aqueous as evidenced by an increased flare of the slit lamp beam traversing the anterior chamber) the prognosis is very bad indeed. Such a condition may be found when previous or active low grade uveitis is noted. It is the impression of most surgeons that the intraocular pressure is reduced after the use of procaine hydrochloride with or without epinephrine given by retrobulbar injection. No accurate research on the degree of fall has been recorded. Probably the fall is due to the shrinkage of the vascular bed of the choroid and ciliary body. With lowered intraocular and retrobulbar pressures there is less tendency for the aqueous to leak or spurt out or for the iris, lens or vitreous to prolapse. The wound does not gape and closes more easily. The intraocular pressure necessarily falls when the eye is opened by the limbus section. All intraocular surgical manipulations are conducted more easily if the tissues are relaxed. If the cornea wrinkles, dimples or even falls in, the conditions are generally favorable for proceeding without danger of loss of vitreous. If the cataractous lens rests posteriorly on a relaxed vitreous fossa it may be difficult to reach, to extract, to tumble and to express, but the conditions are such that an accident, such as loss of vitreous, is not likely to occur. Low intraocular pressure continues after operation until the wound is completely sealed and the anterior chamber is restored. If the formation of the aqueous is retarded or if leakage occurs, hypotony will continue. If the reformation of the anterior chamber is delayed longer than seven to ten days, particularly if the iris, the vitreous or the after-cataract is in contact with the posterior surface of the cornea, complicating anterior synechiae may form. Local anesthesia should be used

and a search made for the leak or wound weakness; if any is found, sutures should be used to close the wound and remedy the fault. Suturing anew or bringing down a conjunctival flap to cover the defect is better than the use of any caustic. Conservative treatment (the use of mydriatics and watchful waiting), however, is always good if with the slit lamp microscope it is discovered that a narrow zone of aqueous exists between the endothelium of the cornea and the iris and other structures.

Detachment of the choroid [7] often is present after cataract extraction. The detachment usually is associated with hypotony and disappears after normal tension is reestablished. I believe that manipulations over the sclera, ciliary body and choroid are a factor in production of detachment of the choroid. It may last for two or three months, however, and be a source of great worry to the patient and to the surgeon. Attention should be directed to correction of the hypotony. If there exists imperfect healing of the incision,[8] a fistulizing cicatrix or a dissecting prolapse of the iris, further evidence of the effect of the hypotony may be present, for example, increased protein in the aqueous, detachment of the choroid or the retina and papilledema. The fistula may be difficult to eradicate, but the cystic cicatrix should be dissected away, the wound edges freshened by curettement, sutures used for apposition of the edges or a flap of conjunctiva reenforced with Tenon's capsule brought down to cover the area of the fistula, the corneal epithelium and Bowman's membrane just below the fistula being removed so that the flap will adhere firmly below the area of the fistula. In some eyes fistulas and filtering cicatrices are seen and the tension is found to be within normal limits. In these there is evidently a tendency to increased intraocular pressure. If the escape of fluid from the inside of the eye is cut off, increased intraocular tension is bound to result and to be rather difficult to treat. Under such circumstances it seems wise not to interfere with the area of drainage unless it is dissecting down onto the cornea and causing edema or opacity of the cornea.

THE USE OF SUTURES IN SURGICAL TREATMENT OF CATARACT

The use of sutures has helped greatly in reducing the incidence of complications in surgical treatment of cataract. Sutures [9] are an advance-

7. O'Brien, C. S.: Detachment of the Choroid After Cataract Extraction, Tr. Am. Ophth. Soc. **33**:325-341, 1935; Further Observations on Detachment of the Choroid after Cataract Operation, ibid. **34**:170-174, 1936.

8. Kirby, D. B.: Fistulizing Cicatrices and Prolapse of the Iris Following Imperfect Healing of the Incision for Extraction of Cataract, Virginia M. Monthly **66**:711-716 (Dec.) 1939.

9. Peter, L. C.: The Stallard Versus Multiple Conjunctival Sutures in Cataract Extraction, Tr. Am. Acad. Ophth. (1940) **45**:46-53 (Jan.-Feb.) 1941. Kirby, D. B., in discussion on Peter.

ment in technic and represent a factor of safety in promotion of healing of the wound, reduction of astigmatism and prevention of hemorrhage and prolapse of the iris. It is agreed that deep sutures coapting the scleral edges of the limbus incision are much more efficient than conjunctival sutures. Even with a single deep central or vertical suture, inaccurate coaptation of edges may result and prolapse of the iris on either side may occur. If such a suture used improperly produces inaccurate apposition it may be worse than none. Three evenly spaced interrupted radial sutures placed in the outer third of the edges of the wound either before the limbus incision, as McLean [10] has described, or after the limbus incision, as has been my habit, are ideal and, although difficult to place, may well be advised and adopted. The use of the binocular loupe for magnification is helpful in their accurate placement.

Placement of Sutures Before the Limbus Incision.—The plea for placement of sutures before the limbus section in the operation for cataract is based chiefly on (1) the desire for correct apposition of the wound edges and (2) the desire to avoid the difficulties and hazards of such manipulation on the opened eye. The arguments against the preplacement of sutures are: 1. There is greater difficulty with the knife section, and the ends of the sutures must be placed far enough apart to permit the surgeon to pass the knife blade accurately between them. It is a nuisance when time has been expended on the suture to have it rendered useless by cutting. Again, if the sutures are placed so far apart that the knife can easily avoid them, there is apt to be buckling, overriding and distortion when they are tied. The Verhoeff track suture and the McLean [10] or the Lancaster [11] method seem admirable for preplacement. They insure accurate apposition afterward. The sutures are inserted in the dense corneal and scleral tissue. They go through and not over the lips of the wound and give correct appositional closure. If in any case it seems difficult to insure a proper section without cutting the suture thread with the Graefe knife the surgeon may use a keratome, easily inserting the point and the blade between the suture, and then complete the section with the scissors. The incision thus made heals well; there is no interference with the nutrition or the transparency of the cornea, and there is no astigmatic aberration or other fault which may be attributed to the scissors section.

Sutures in loose conjunctivas are hardly better than none. In the insertion of a deep suture, such as the Stallard [12] suture, it seems to me

10. McLean, J. M.: New Corneo-Scleral Suture, Arch. Ophth. **23**:554-559 (March) 1940.

11. Lancaster, W. B.: Personal communication to the author.

12. Stallard, H. B.: A Corneo-Scleral Suture in Cataract Extraction, Brit. J. Ophth. **22**:269, 1938.

logical that dissection of the conjunctiva from the central area of the upper limbus should be performed to bare the episclera and the sclera for insertion of the upper limbus of the suture. The ends of the sutures can be passed through the conjunctiva before tying in order to avoid burying the knot. Passage of the needle through the relatively bulky conjunctival and subconjunctival tissues is inaccurate. The tying of a suture the points of entrance of which are 4 mm. apart (2 mm. below the limbus for one and 2 mm. above the limbus for the other) may buckle the tissues and cause them to invert, override or distort unless care is used in applying just the right tension for apposition. The diagonally sliced deep limbus tissue is necessarily coapted on a diagonal plane, and, particularly with the anterior chamber empty, as it is after the operation, the edges will tend to override unless part of the suture is through the very margins or lips of the wound as in the interrupted radial sutures.

Personal Experience with Sutures.—I have tried the various needles and materials which are available, and I like the cutting needles on ½ or ⅜ curve the best. The sclera and the cornea are tough tissues, resistant to needle puncture, and are perforated better by cutting than by a rounded needle edge and body. In general a medium length needle is better than a long one. I have been satisfied with a small, specially made ⅜ curve needle measuring 10 mm. between the tip and the end, with the area just behind the center flattened for better grasp, so that the needle will not turn in the needle holder. The suture material which seems best is six zero firmly braided barbless black natural silk with long fibers running away from the needle. If the suture is difficult to draw through the tissues or if there is any tendency for the thread to bunch the thread should be better and smoother in quality. The insertion of the thread into the end of an atraumatic needle by pressure rather than by screw tip gives the least bulk. The doubling of the thread in the eye of any needle which requires threading increases the difficulty of pulling this end of the needle through and represents a hazard in its use. For the quality of sharpness, a needle must be of small caliber, of the cutting type and of high temper. The last-mentioned feature often is accompanied with brittleness and fragility. If the sutures were deep this would be a real danger, but in superficial suturing, such as that required for the outer third of the lips of the cataract section, the two parts of a broken needle can always easily be recovered. However, perfect needles should not break. Surgeons should not accept defective needles and should regularly examine their sutures, needles and instruments under magnification for defects. The chief cause of breakage of otherwise perfect needles is failure of the user to follow the curve of the needle in insertion and withdrawal.

Three interrupted sutures should be placed equidistant from each other at 10:30, 12 and 1:30 o'clock on the schematic corneal dial and from the ends of the limbus section, which includes two fifths to one half of the circumference of the limbus. The accuracy of radial insertion can be well judged by the trained eye. The chief mistake making for inaccuracy and malposition is the tendency to run the suture vertically instead of radially. Thus a suture inserted in the edge of the corneal flap at 10:30 on the clock dial should enter the scleral edge not at 11 o'clock but at 10:30, and the same precaution should be taken for the opposite suture. The suture at the vertical meridian at 12 o'clock is usually accurately placed, for obvious reasons. The lateral sutures require shifting of the position of the body and arm to obtain accurate radial placement. The use of a good forceps for picking up and holding the edge of the wound is important. Such a forceps should be strong and should have good teeth which will grasp the outer edge of the tissue without slipping and without undue trauma. It is well to have a guide between the blades of the forceps, so that they will not buckle or turn. The needle should be passed close to the bite of the forceps, so that the tissues will not turn under the insertion of the needle. Ring-tipped forceps have been tried but are not satisfactory.

The two lateral sutures, having been placed through both the limbus and the scleral edges to a depth of about one third of the thickness of the tissue, are then drawn through so that there will be a convenient loose short end (about 3 to 4 cm.). A single loop is made in each before they are laid aside in orderly fashion for convenient tying. The third, or central, vertical suture is placed in the limbus of the cornea and not through the scleral edge until the completion of the operation. It may, however, be passed through the scleral edge if the surgeon wishes to have this completed before the lens is extracted. This central suture is drawn through to half its length and is first used as a traction suture for elevation of the corneal flap to afford a direct view of the iris and the lens capsule. In my experience careful elevation or turning of the corneal flap does no harm. It is well to make sure that the iris is not caught between the lips of the wound before the appositional sutures are drawn tight, because it is difficult to free the iris when it is so incarcerated. The sutures should be tied with a square knot and reenforced by a third turn. The tension of the suture should be just enough to appose the wound edge correctly and not enough to cut through the tissues.

The danger of injury to the ciliary body and to the root of the iris and the possibility of devitalization of tissue must be remembered in the insertion of deep sutures, as must the possibility of infection in tissues of low vitality, such as the cornea and the sclera, particularly in elderly persons with low resistance to infection. In some hands and

with some needles considerable difficulty with fixation and with passage of the needle through the dense cornea and the sclera may be experienced. The advantages of the use of deep sutures and the closure of the wound far outweigh the disadvantages, but judgment must be used, as these procedures are not necessary in all cases.

The test for efficiency of suturing may well be the ability of the anterior chamber to hold fluid, which may be pumped in under gentle pressure. In about a dozen cases I have injected into the anterior chamber a small bubble of sterile air after tying the suture, the reason being that if the chamber is air tight it is also water tight. I have thought that the air, being light in weight as compared with fluid, such as physiologic solution of sodium chloride, would tend less to carry out the iris in case of its escape. No undue reaction followed the introduction of the bubble of air. There was no danger of interference with the nutrition of the cornea, because fluid existed between the air and the endothelium. The efficiency of the method of suturing was established.

A word about the removal of sutures after healing is important. Fine material placed in dense tissue naturally has a tendency to cut through somewhat over a period of days. If an attempt is made to remove scleral sutures too early there may be undue difficulty and perhaps a regrettable accident, such as opening of the wound, hemorrhage or even loss of vitreous. There is no great hazard in leaving the sutures, particularly in nervous and sensitive patients, for ten to twelve days. Then the surgeon will do well to make sure of sufficient anesthesia for their painless removal. I make it a practice to instil 3 drops of 0.5 per cent solution of pontocaine hydrochloride at thee minute intervals and then, with the patient recumbent, to put a few minute grains of powdered cocaine or phenacaine or a few flakes of pontocaine niphanoid on the tissues near the suture. This insures complete anesthesia of the tissues near the sutures.

TECHNIC OF TREATING VARIOUS COMPLICATIONS

Corneal Opacity and Dystrophy.—The cornea, being normally avascular, depends for its nutrition on circulation of a clear lymph through the stroma and on the lacrimal and anterior chamber fluids. The incision in the limbus of the cornea, extending from two fifths to one half of the circumference, must interfere greatly with the nutrition. After healing of the incision the function of passing the clear lymph through this area into the corneal stroma is undoubtedly recovered. If the endothelium and Descemet's membrane are injured, the aqueous humor of the anterior chamber may abnormally enter the stroma of the cornea and cause edema and opacity. An important point in intraocular surgical procedures is the avoidance of injury to the endothelium of the cornea. The surgeon should take care not to touch even the backs of

the instruments to the endothelium. Inflammation, either bacterial or chemical in origin, may contribute. Continued and excessive irrigation of the anterior chamber may injure the endothelium. I believe that this type of injury is responsible in many cases for edema of the cornea and striped keratitis. If healing of the breach does not occur, dystrophy and bullous keratitis may develop.

I have found that it is well worth while to lift or retract the corneal flap [13] to protect the endothelium of the cornea and to afford a direct view of the iris and the lens capsule for the necessary manipulations. This has been found to be a conservative procedure and may well be recommended. It is best to do it with a centrally placed suture and not with a forceps. When a forceps has been used, the surgeon has been observed to pick up and drop the flap several times during an operation, thus producing unnecessary trauma. The turning of the corneal flap has never added an element of danger to the operation and has not of itself produced striped keratitis or any form of corneal opacity. I believe that it is better to see what one is doing to the iris and the lens capsule than to be guided falsely or poorly by the appearance of these structures through the hazy, wrinkled, relaxed cornea. Blood clots can be picked out from the anterior chamber, the peripheral iridotomy can be placed accurately and the lens capsule can be picked up gently and without disturbing the bulk of the lens and without any fear of dislocating the lens. The act of picking up the capsule in this manner does not carry with it the danger of pushing it back into the vitreous by unnecessary pressure.

In cases in which dystrophy of the cornea due to nervous, nutritional or other disorders is present before an operation for cataract, complications in the healing process with resulting opacity, edema or bullous keratitis may develop. The prognosis for dystrophy of the cornea is not good unless the condition is due to a vitamin deficiency which may be remedied. Vitamins A, B (the entire complex) and C all seem important for the health of the cornea and should be administered in large quantities if there is any suspicion of deficiency. No direct effort can be made to heal a breach in the endothelium and in Descemet's membrane. A firm dressing may be applied over the closed eyelids. If the intraocular tension is normal or above normal limits paracentesis in the periphery of the cornea may help the lesion in the endothelium to close and heal. Established bullous keratitis after cataract extraction may show some improvement after removal of the diseased epithelium, curettement of Bowman's membrane, application of half strength tincture of iodine and the use of a firm dressing over the

13. Kirby, D. B.: A Technique for Intracapsular Extraction of Cataract, Am. J. Ophth. **19**:1006 (Nov.) 1936.

closed eyelids. Recurrence of the bullae is bound to occur unless the deeper cause is remedied, and this is not always possible.

Corneal Opacities.—Dense central corneal opacities present in cases of cataract require optic iridectomy or keratoplasty before the cataract is removed. The latter procedure is difficult when the eye is aphakic.

Arcus senilis, gerontoxon and opacities following ulcers of the limbus may cause some deception in the making of a proper limbus section. The surgeon should orient himself in relation to the true limbus. Macular or nebular opacities of the cornea do not require any special reference.

Opacity of the cornea following operation may be due to infection, inflammation, trauma to the endothelium or downgrowth of epithelium. The prevention and treatment of these conditions are considered under the appropriate titles.

Hemorrhage.—A survey of the general condition before operation should be helpful in detecting patients in whom a tendency to hemorrhage is present. In patients with vascular hypertension, if the systolic pressure is high and the diastolic pressure normal improvement and satisfactory preparation for operation may be obtained by sedation and by rest in bed. A high diastolic pressure gives a graver prognosis because of the increased pressure in the vascular bed of the uvea. Blood counts, tests of the bleeding and coagulating time, estimation of the fragility of the capillaries by the pressure cuff or the suction cup method and estimation of the blood vitamin C level, the blood sugar level, etc., may give certain information according to which the surgeon may take a definite course of action, but in general the results of treatment are unsatisfactory. The administration of vitamin K before operation may prove to be of value in certain cases. Further research on the processes of bleeding and coagulation may give better leads. Except in cases of purpura and allied conditions, testing with moccasin snake venom [14] and treatment by immunization have proved unsatisfactory and fruitless. It is fortunate that active arterial bleeding is not often encountered in intraocular surgical operation and that rupture of veins with large subchoroidal hemorrhage or with expulsive hemorrhage from the choroid is very infrequent. In the face of such a disaster, after preliminary precautions have been taken not much can be done. Proper diet, rest, sedation, phlebotomy (for plethoric persons only), the lowest degree of surgical trauma, care not to make the limbus section too deep, the use of vasoconstrictors, such as epinephrine and epinephrine bitartrate solution, and, finally, efficient wound suturing are all excellent measures to prevent hemorrhage. The electrocoagulation current may be kept ready

14. Alvaro, M. E.: Snake Venom in Ophthalmology, Tr. Am. Acad. Ophth. **43**: 304-329, 1938.

for sealing a persistently oozing vessel in the limbus section but is not to be recommended for routine use. If oozing of blood from the limbus section occurs it is well to stop manipulations for a few minutes to rest the parts and to give the blood a chance to coagulate. The same may be said of hemorrhage in the anterior chamber. Bloody fluid and clots obscure the field of operation and render inaccurate the operative maneuvers. If the blood is allowed to form into a firm clot it may be picked out with a forceps. The bloody fluid may then be easily washed out with physiologic solution of sodium chloride and a clear field of operation reestablished.

Absorption of Blood.—The absorption of a small amount of blood left in the anterior chamber after operation occurs rapidly in the average person. In some patients it may be delayed, and, particularly if blood fibrin is mixed with the products of inflammation and with retained cortex, a secondary cataract, or after-cataract, will form which will require discission later.

If during the injection of the local anesthetic a severe subconjunctival hemorrhage develops, this may prove so embarrassing that it is best to postpone operation. If retrobulbar bleeding occurs postponement of the operation is necessary. It is surprising that in elderly persons with sclerotic arterial and venous walls hemorrhage from this source does not occur more often. The veins do not slide out of the way of the needle as it is passed back into the orbit, and even though suction is made with the syringe to make sure one is not in a vein (so that the procaine hydrochloride will not be injected into the vein rather than into the orbital tissues) bleeding may occur from a vein which has been pierced by the needle. Under such circumstances it may be well to omit the retrobulbar injection in the second attempt.

Prevention of Hemorrhage During Injection of Procaine Hydrochloride.—My attention was drawn [14a] to the method of forcing a small amount of procaine hydrochloride ahead of the needle point as it is advanced for induction of local anesthesia by injection. The point of the needle is advanced into this fluid, which forces the vessels out of the path. Thus one can be sure that one does not injure the wall of or pierce any vessel and that one will not encounter any embarrassing hemorrhages.

The complication of embarrassing subconjunctival and retrobulbar hemorrhages has been spoken of under the appropriate title. If the injection of procaine hydrochloride produces edema around the cornea it may interfere with the puncture and counterpuncture. The injection should be made into Tenon's capsule above and below, away from the corneal limbus.

14a. Gailey, W., and Duane, J.: Personal communication to the author.

Secondary Hemorrhage.—Secondary hemorrhage may occur at any time, either spontaneously or during manipulation. It may occur during dressing, during removal of sutures or during interference by the patient or by others. Hemorrhage is usually accompanied with a sharp pain, and if this occurs during sleep the patient is apt to awaken with his finger or his hand near his eye and to attribute the pain to his having unconsciously meddled with the eye. The true sequence of events is probably the happening first of the spontaneous hemorrhage; then the coincidental pain, and finally the natural reflex of bringing the hand to the eye, all these events occurring before the patient is fully awakened. In dressing the eye the surgeon should bear in mind the freshness of the operative wounds and should be very cautious about any maneuver which is likely to cause a secondary hemorrhage. It is hardly necessary to do anything about a small secondary hemorrhage into the anterior chamber except to have the patient rest and to use various general methods which will help the hemorrhage to absorb. The use of potassium iodide and of a diet high in vitamins and other measures may be of value. One or two small bleedings into the anterior chamber may not influence the end result, but they are not desirable by any means. Sutures should not be removed too early, and when they are removed local anesthesia should be efficient and the patient relaxed.

Thrombosis.—Seldom if ever has retinal venous thrombosis or arterial occlusion been observed directly in connection with ocular operations, although it may and probably does occur. Observations have been made which link venous thrombosis following general anesthesia with dehydration and chemical changes in the blood. It is well to make sure that this does not occur after any general anesthesia and to use plenty of fluid by all portals, even by hypodermoclysis, if there is any dehydration. This precaution will hardly ever apply to cataract removal.

The Size of the Limbus Section for Extraction of Cataract.—The size of the limbus section is important. An estimation of the size of the cataract and of the hard nucleus may be made by various criteria before the operation and the size of the incision gaged accordingly. If the chamber is shallow a small knife section and enlargement with scissors are indicated. If the surgeon is timid it is better for him to make a small section confidently and enlarge it with scissors than to start a large section and fail to complete it. Properly made scissor sections heal well, without opacity or other evidence of trauma. Conjunctival frills are important at the sides but not so necessary at the top if sutures are used to bring the conjunctiva over the incision.

Prolapse of the Iris.—If the aqueous seeps out and the iris prolapses on the blade of the knife during the section it is better to withdraw the knife and complete the section with the scissors than to haggle

the iris. It is well also not to attempt to open the lens capsule with the knife on the limbus section.

If the iris prolapses immediately after the section has been completed it may indicate increased intraocular or retrobulbar pressure. An examination should determine which factor is active, and if there is pressure on the globe, particularly at the equator, by the lids an external canthotomy should be done. One should not proceed further without this if the indications are that it will help. An attempt to replace the prolapsed iris may show that it is relaxed and under no pressure. If the iris persists in prolapsing, complete iridectomy is indicated.

Handling of the Iris.—Peripheral iridectomy or iridotomy may be done when the iris is relaxed. One purpose of cutting the iris for formation of either a complete or a partial coloboma is to form a channel of communication between the posterior and the anterior chamber, so that if there is any escape of aqueous from the anterior chamber through the wound it will not carry with it the base of the iris in a prolapse, even though it makes its exit in a gush. An opening through the iris will be effective only if it is in the periphery. To place it in the periphery one must see the base of the iris. This can be done if one lifts the corneal flap. One will discover a limbus shelf if it exists and be able to reach around it to pick up the iris. It is best to carry the point of the iris picked up toward the center of the pupil and at the same time to "tent" it by lifting it off the lens capsule and the zonular fibers; then one should cut behind the point where the forceps holds the iris. These steps insure a peripheral opening without danger of injury to the lens, the zonule or the vitreous.

The opening in the iris made by peripheral iridotomy is as satisfactory as that made by peripheral iridectomy.

Complete Iridectomy.—Complete iridectomy is definitely indicated when the iris is rigid and the pupil will not dilate well. It may also be used to facilitate the delivery of the cataract and to help in preventing an embarrassing cystic dissecting prolapse of the iris. However, the pillars of the iris coloboma may prolapse and be incarcerated in the lips of the wound. The iris does not and cannot hold back the vitreous in danger of prolapse, but a good round pupil in an iris which is in its proper plane after extraction helps to keep the vitreous in better position after healing. There is in the average case less vitreous in the anterior chamber in the presence of a round pupil than in the presence of coloboma.

If the pupil as tested by the instillation of 3 drops of a 2 per cent solution of a homatropine salt at intervals of ten minutes will dilate to 6 mm. or more, a cataract up to 10 mm. in diameter will pass through it. If the pupil will dilate only to 5 mm. only a smaller cata-

ract will pass, while if the pupil will not open more than 4 mm. a complete coloboma is definitely indicated.

At the conclusion of a successful intracapsular operation, whether there is a complete coloboma or a round pupil, the use of 1 per cent physostigmine sulfate solution is indicated to draw the iris into the chamber and to keep it from being incarcerated in the lips of the incision. At the time of the first dressing atropine may or may not be employed, according to indications. Atropine sulfate solution in strengths varying from 1 to 3 per cent is generally indicated in extracapsular procedures. Its general employment may be an indication of the frequency of iridocyclitis.

Iris Synechiae.—Where posterior synechiae exist as evidence of old iritis with adhesions to the anterior portion of the lens capsule, separation of the synechiae from the capsule may be made with the flat iris spatula before the lens is extracted. If the pupil is dilatable after the synechiae are freed, the lens may be removed through the round pupil; otherwise an iridectomy coloboma must be made. If there are anterior synechiae due to congenital anomalies or to preexisting glaucoma, trauma or preliminary iridectomy, the incision must be placed anteriorly to avoid cutting the iris at its attachment to the endothelium. When such an incision is necessary, fine sutures may be placed between the lips of the corneal section.

Replacement of the Iris.—In replacing the iris it is well to introduce the iris spatula over the iris and not through the coloboma and to keep the spatula on the iris and not allow it to slip off into the pupillary area, thus avoiding the danger of injuring the posterior part of the capsule or the hyaloid membrane of the vitreous. The iris spatula should have a malleable blade so that it may be bent 7 mm. from the end at an obtuse angle of about 110 degrees between the upper portion of the blade and the shank of the instrument. A rotary movement imparted to a cylindric [15] handle carrying the point around and toward the center of the pupil is best adapted to the reposition of the pillars of the iris when a complete coloboma has been made. The patient may be moved from the operating table to the carriage and then to his bed with relative immunity from danger of prolapse of the iris immediately after operation, because of the absence of fluid in the anterior chamber.

The Handling of Prolapse of the Iris.—The danger of prolapse arises when the anterior chamber has reformed. The aqueous may gush out if the wound is opened. If this happens and the prolapse is

15. Kirby, D. B.: Instruments for Cataract Operations: Cylindrical Handles; Matched or Related Instruments, Am. J. Ophth. **12**:120-121, 1929; Cylindrical Handles on Instruments for Cataract Operation, Tr. Am. Acad. Ophth., 1928, vol. 33.

discovered within twenty-four hours of its occurrence and if the iris is covered by conjunctiva, the iris may be found nonadherent, and an attempt may be made to replace it within the anterior chamber. If the iris has been exposed and not covered by conjunctiva, it may be judged best to excise the prolapsed portion, free the pillars and replace them in the anterior chamber. Physostigmine salt in aqueous solution may be employed to aid in the reposition. If the iris has been out more than twenty-four hours it is probably covered and bound down by fibrin and will require blunt dissection and excision. If the prolapsed iris is flat and the aqueous seeps out along the tract the prolapse may not extend or increase, but if the iris is ballooned out by the aqueous it will probably go on to dissecting prolapse, extend farther and cause a fistulous opening and subconjunctival communication with the anterior chamber. In such a case if excision for any reason cannot be done early, at least an opening should be made in the ballooned area to stop the dissecting process. Complete local anesthesia should be used, and in some cases even avertin with amylene hydrate or intravenous pentothal sodium is necessary because of tenderness which may develop as a result of an inflammatory reaction. If the prolapse is old and cystic it will require dissection, excision, freshening of the edges of the wound and closure by sutures. Under the heading of glaucoma it was shown that if there is an indication that the old cystic prolapse is a release valve or a filtering cicatrix to keep the pressure down it may be unwise to interfere with this filtering area. The application of caustics, such as trichloroacetic acid, to a prolapsed iris, particularly if it is covered by conjunctiva, is ineffective and dangerous. The use of the electrocoagulating current with the blunt electrode will prove satisfactory in reducing small prolapses when iridectomy is not indicated.

PROLAPSE AND LOSS OF VITREOUS

Preoperative Examination.—The preoperative examination may reveal abnormal fluidity of the vitreous, a degeneration of the ordinary viscous gel to a semifluid substance in which opacities are observed to fly about on movement of the eye. In such cases great concern is justly expressed regarding the danger of loss of vitreous, but if a small amount of fluid vitreous escapes the eye may heal and do well. The loss of fluid vitreous is similar to the loss of aqueous and is easily replaced. However, there is no "laudable vitreous," no "laudable loss of vitreous" and no condition in which in the ordinary eye with cataract there is "too much vitreous." Any presentation, incarceration or loss of vitreous is to be regretted. It is to be avoided if possible.

Subluxation and Dislocation of the Lens in Relation to Loss of Vitreous.—Examination preliminary to the operation of extraction of cataract may reveal conditions which would indicate greater than average

danger of loss of vitreous. There are eyes which through congenital anomaly, trauma or degeneration exhibit the presence of vitreous in the anterior chamber. Such conditions as subluxation or dislocation of the lens require definite preparation for loss of vitreous, although it need not occur. The preparations include three preplaced limbus appositional sutures, looped once and ready for closure, and a wide iridectomy so that after the extraction without the maneuver of reposition of the iris pillars there will be nothing between the lips of the wound except possibly the vitreous. The accepted technic of removal of dislocated lenses by "looping them out" necessarily involves loss of vitreous. I have demonstrated in several cases that subluxated lenses need not be looped out. Direct view of the lens capsule must be had by drawing the corneal flap downward, so that the forceps may be placed delicately and accurately on the capsule, a proper portion of the capsule being picked up without the necessity (or the mistake) of pressing back on the body of the lens. A few subluxated cataracts arising from congenital malformation or from trauma have been removed by adopting the method of forceps application under direct view and without looping them out. With such cataracts the preliminary examination may and usually does indicate by the position of the lens the zonular fibers which are still intact. It may be necessary to do an iridectomy. The lens capsule is gently picked up with the forceps, which should be accurately applied without pressure. The lens is then carried radially to the central area to expose the zonular fibers which are still intact. These are divided as easily as possible. Various forms of zonulotomes have been devised, but the safest is probably the blunt elbow of the lens hook ordinarily used for pressure in intracapsular extraction. With this the fibers are rubbed off from their attachment at the equator. In 2 cases of this type of cataract in which no loss of vitreous had occurred the iris became drawn up and disappeared behind the limbus. This development indicated that probably the vitreous had become incarcerated in the limbus incision. The mechanism of this same coloboma formation and disappearance of a portion of the iris when vitreous has been lost is interesting and probably depends on contraction.

Retrobulbar and Equatorial Pressure as Potent Causes of Loss of Vitreous.—A frequent cause of loss of vitreous is pressure from the retrobulbar tissues on the posterior segment of the globe or pressure from the ring of the lid margins and the canthal ligaments on the equator. The former may be encountered in cases of exophthalmos. Embarrassing proptosis may be found in cases of hyperthyroidism and in some cases of hypothyroidism. It may also be met when a neoplasm or trauma has added to the bulk of the orbital tissues, when too much procaine hydrochloride or other local anesthetic solution has been introduced, or when introduction of the needle has caused transudation

or hemorrhage from the orbital vessels. Improper introduction of the needle into the orbit may cause bleeding by tearing the wall of a vein or by piercing the vein. Normal veins would ordinarily elude the point of the needle, sliding out of the way, but when the veins are sclerosed, and particularly when they are congested, they are apt to be injured. In the presence of sclerosis and/or congestion, therefore, it may be well to avoid the use of any retrobulbar injection. Increased retrobulbar pressure or tight palpebral fissures must be detected before the limbus incision has been made. After the introduction of the speculum or the lid retractor, their effect on the globe is noted. If the lids are relaxed and entirely free from the globe, all is well. However, if manipulation of the speculum or the retractor discloses pressure on the globe, external canthotomy is indicated. In cases of mild involvement simply a horizontal section elongating the fissure will relieve the pressure. However, if after this has been done there is still pressure, vertical subcutaneous section of the external canthal ligament above and below the horizontal section, finally severing it from its attachment to the periosteum of the lateral orbital wall, is necessary. In some cases it may be necessary to use rather extreme measures. Incision of the orbital fascia may finally be resorted to in a few cases, resulting in prolapse; if this is embarrassing, removal of some of the orbital fat may be done. In all cases in which more than a simple horizontal incision is made in the external canthus, appositional sutures and in some cases deep sutures are necessary.

Superior Rectus Traction Suture in Relation to Loss of Vitreous.—In the consideration of pressure on the globe as the cause of loss of vitreous one must discuss the use of the superior rectus traction suture, which is employed to assist in the downward rotation of the globe. If this suture is used it should be placed well back in the belly of the muscle, so that when it is drawn down it will simply temporarily loop and disable the superior rectus muscle and thus prevent the patient from using it to look upward. One should, however, not forget the powerful action of the inferior oblique muscle, which the patient may use for the same purpose. Generally surgeons who use the superior rectus traction suture place it at or near the insertion of the muscle into the sclera, and some even draw it down and clamp it to the speculum or to the sterile drapery. If it is used in this way there are definite traction and pressure on the globe, which may be dangerous. There is greater facility in delivery of the lens when the cornea and the limbus incision are kept within the palpebral fissure, but rather than use a superior rectus traction suture to keep the eye of a noncooperative and unruly patient there I prefer to inject procaine hydrochloride into the superior rectus and the inferior oblique muscle and thus diminish their action as elevators. Finally I should advocate

delivery of the lens with the eye rolled up under the upper eyelid, the lid being elevated with the speculum, with the lid hook or with the retractor, rather than drawing down of the eye with a suture in the sclera or in the insertion of the superior rectus muscle.

Preoperative Sedation and Relaxation of the Patient in Relation to Loss of Vitreous.—If effort and time are expended on the average patient, his cooperation and relaxation will be secured. Generally the lack of these is induced by fear of the unknown and of failure of the operation and consequent blindness and by lack of confidence in his own ability or that of the surgeon to carry through successfully.

Introduction of patients who have been successfully operated on by the surgeon in charge and the detailing of their experiences to candidates for operation usually have a most salutary effect. The intraocular tension should be tested with the tonometer with the patient lying down, and at that time the patient should be given a little instruction in the matter of "looking down." Probably the order "look down" does not convey the proper impression to the patient. If he is not instructed to "keep both eyes open" at the same time he usually attempts to shut the eye which is not being operated on, and that causes both eyes to roll upward. A better order is "look at your feet" or "look at the light" (a light of low intensity and of different color [probably red is best] having been placed near the foot of the table).

For the relief of excitement, nervous tension and worry, preoperative sedation with drugs of the barbital group is excellent. Opium and its derivatives should be avoided. With good cooperation local anesthesia is preferable to general anesthesia, although the latter (if possible induced by intravenously injected pentothal sodium or by colonic avertin with amylene hydrate alone or by other narcotic drugs) has gained some adherents.

The most gentle handling, particularly in the initial injections for local anesthesia, is important. Encouraging remarks and the avoidance of irrelevant conversation within earshot of the patient, particularly of disquieting remarks, are necessary. I have found that the orders "Take a deep breath," "Now let it out," and "Now take another deep breath" aid greatly in producing relaxation. The admonitions "Don't hold your breath," "Don't move your eyes," "Don't squeeze," etc., usually fail, chiefly because of the negation. For successful response to orders under trying conditions the orders must be in the affirmative. If the patient loses his head and becomes unruly it is best for the surgeon to keep his patience, remove the speculum and allow the patient to rest a while before proceeding. Forbearance and patience will be rewarded.

"One Hand Does Not Always Know What the Other Hand is Doing"; Prevention of Loss of Vitreous.—A habit of some surgeons in

performing extracapsular extractions is to use a spoon, a loop or some other instrument with the left hand to hold back the posterior edge of the incision. The following reasons are given: "to assist in delivery of the lens by widening the wound opening posteriorly" and "to support the vitreous." I believe that the unguided use and placement of an instrument in this area by the left hand is dangerous. Particularly, as it seldom accomplishes anything, an instrument should not be placed on the sclera prior to or during the manipulation with the expressor instrument used in the other (right) hand, because the surgeon becomes so interested in the action of the latter that he often does not know what is being done by the instrument in the left hand. I believe that if in an extracapsular extraction the surgeon will hold the speculum or the upper lid retractor with the left hand and keep the lids free from any pressure on the globe he will use his left hand to the best advantage. Only when it is necessary to use a loop should he turn over to the assistant the handling of the speculum, take a spoon or a hook in the right hand and use the loop in the left hand.

Looping Out of a Subluxated or a Dislocated Lens; Prevention of Excessive Loss of Vitreous.—The manner of looping out a subluxated or dislocated lens deserves description. The loop held by the left hand should be started vertically and carried under but close to the posterior surface of the cataract, with the least possible disturbance of the anterior portion of the vitreous. The practice of a wide sweep of the loop through the vitreous should be discouraged. After the cataract has been engaged on the loop and carried up so that it fits into the concavity of the posterior surface of the cornea it should be steadied there and expressed by pressure from without with the spoon held by the right hand. Only when this is not feasible should the loop draw out the cataract. After the cataract has been expressed, the loop may be slid out with a minimum of loss of vitreous. Needless to say, a lens which is almost or completely dislocated and has sunk well into the vitreous presents a most serious problem, and it may be best judgment not to go in after it; the bad effects of allowing it to remain are preferable to the certain ruin of the eye caused by insistence on its immediate removal together with a great mass of vitreous. The phenomenon of fluorescence of the crystalline lens when illuminated by ultraviolet rays [15a] passed through a filter is of value in the location of remnants of cortex and of subluxated or dislocated lenses.

Necessity of Loop Extraction.—If vitreous is in the anterior chamber before the incision or comes into the anterior chamber immediately after the incision (as may be noted by deepening of the anterior chamber

15a. Hildreth, H. R.: A Surgical Ultraviolet Lamp as an Aid to the Removal of Dislocated Lenses, Am. J. Ophth. **17**:414-416 (May) 1934. Hague, E. B.: A New Ultraviolet Lamp for Cataract Surgery, ibid. **23**:317-318 (March) 1940.

which was emptied of the aqueous by the incision) or if vitreous presents in the wound before the cataract has been extracted, there is no recourse except removal of the cataract with the loop.

Increased Intraocular (Intravitreous) Pressure in Relation to Loss of Vitreous.—The intraocular tension and any tendency to increased pressure should be known before operation. One may be surprised, however, in cases in which the tonometer gave a normal reading before operation, to discover immediately after the incision that instead of the desired condition of relaxation, with irregular wrinkling, crumpling or falling in of the cornea indicating absence of undue posterior pressure, there are gaping of the lips of the wound and a crease across the cornea between the puncture and the counterpuncture. This picture is bad and is an ominous sign of probable loss of vitreous. Steps should be taken immediately to relieve any external pressure. If there is none, increased choroidal and/or increased intravitreous pressure is present. It may even portend an expulsive hemorrhage from the choroid. If this is not happening and one has relieved the external pressure, there is no course open except to proceed, being ready to tie the sutures to close the eye immediately after the extraction. Some say that this condition is a direct contraindication to intracapsular extraction. The sutures should be in the firm scleral tissues and not simply in the conjunctiva. It is not necessary always to be ready to tie the sutures immediately after an uncomplicated extraction. It is best to replace the iris pillars carefully and not to permit them to be incarcerated in the lips of the wound. To be fearful that in every case uncontrolled loss of vitreous may occur and to have as the only defense the hurried closure of the eye by sutures is "grim surgery," as Wright [16] has aptly put it. But to have preplaced sutures ready to close the eye in cases in which pressure is known to be present or in which it develops unexpectedly is a worth while safety procedure.

Prevention of Loss of Vitreous After Extracapsular Extraction.—If the cataract has been removed by the extracapsular method, one must decide by the appearance of the pupillary area and by the use of filtered ultraviolet radiation how much of the free cortex remains in the eye. One may use irrigation to remove decomposed, flocculent gray or white cortical debris, but sticky or clear lens cortex cannot be irrigated away safely. It requires the lytic action of the aqueous and the lens ferments for its decomposition and absorption. One may introduce a flat spoon as Elschnig did, but one must be sure not to injure the posterior capsule, the hyaloid membrane or the endothelium of the

16. Wright, R. E.: Lectures on Cataract: I. Am. J. Ophth. **20**:1-12 (Jan.) 1937; II. Difficulties at Time of Cataract Operation, ibid. **20**:119-131 (Feb.) 1937; Anterior-Segment and Other Complications in Post-Operative Period, ibid. **20**: 240-253 (March) 1937.

cornea. If one employs an irrigator, the principles of not introducing the tip through the coloboma area, of keeping the tip of the irrigator and the stream of physiologic solution of sodium chloride on the iris and of not persisting too long or too vigorously in the irrigation should be remembered and practiced.

Presentation of Vitreous After Extracapsular or Intracapsular Extraction.—If vitreous presents even in a small bead after extraction by either the extracapsular or the intracapsular method, necessarily all the manipulations for irrigation and reposition of the iris must stop for the time being, and as much relaxation of the ocular tissues as possible must be induced. The speculum should be removed carefully and without undue agitation. It is well not to alarm the patient by any sudden move, exclamation, reproof or accusation. The eyes may be closed carefully; one should place the upper lid over the cornea and make sure that the edge of the lid does not catch the upper lip of the incision. If all goes well the bead of vitreous may recede into the eye after a period of rest. Then the toilet of the iris and of the wound edges and the tying of the sutures may be completed.

Prolapse of Vitreous and Loss of Vitreous.—If, however, attempts to induce relaxation do not succeed and vitreous is prolapsed or lost, there is no recourse except to deal with the situation as presented. The loss of fluid vitreous from the anterior chamber may not have any bad effects, either immediate or late, but the prolapse and loss of vitreous gel is more difficult to handle. One cannot well permit the wound to remain gaping open and send the patient to bed with the eye thus exposed. The result at best would be a deformed cornea with a large astigmatic aberration, a partially healed wound, an incarcerated iris and an updrawn pupil, with great danger of infection, inflammation, opacity of the vitreous and other subsequent complications. If one does not have preplaced sutures one may be forced to submit, because the placement of sutures under these conditions might result only in disaster. The tying of good sutures will result in closure of the wound. If the vitreous is fluid or semifluid there may be none of it between the edges of the wound, but if it is of normal viscosity it will be necessary to excise the portion which protrudes. An attempt should then be made to replace the iris. Replacement of the iris is resisted by the vitreous, and even though the iris seems to have been replaced successfully it will appear drawn up into the wound area after the latter has healed. If the wound can be closed and healing induced without inflammation or infection, the eye may prove useful.

Some operators say that when the iris is drawn up in hammock form well up above the visual line they use a discission knife vertically to cut the sphincter of the iris and to provide a pupillary opening.

Disturbance of the Vitreous After Discission.—The consideration of behavior of the vitreous on discission for after-cataract is interesting. The membrane which develops secondary to removal of cataract by the extracapsular technic is composed of lens capsule cortex, fibrin and secondary cicatricial tissue. A potential or a real space separates it from the capsulozonular barrier. This space is too narrow even to permit division of the membrane without division also of the posterior lens capsule and the hyaloid membrane. The use of the Knapp or the Ziegler knife is said by some to be effective in dividing the membrane without injuring the hyaloid membrane when it is insinuated between the two, but this is to be doubted when one considers the pathologic anatomy of the structures. In the use of the de Wecker scissors and the Wheeler discission knife, no pretense is made about not disturbing the vitreous. The Wheeler knife puncture is made about 1 or 2 mm. inside the clear limbus of the cornea, the point of the knife being passed down across the anterior chamber until it punctures the lower part of the membrane; then by rapid, careful diagonal slicing, effectively and with the least trauma, the strands of the membrane are cut across in such a manner that a separation is made to form a pupil. Necessarily the path of the knife is partly through the vitreous, and vitreous may cling to the point of the knife as it is withdrawn unless the knife is lifted fairly straight up through the aqueous, the vitreous being dropped off the point as the latter traverses the aqueous and before it emerges from the cornea.

Protrusion of Vitreous Through Incision in the Cornea.—In rare instances the vitreous framework and gel become incarcerated in the opening made by the discission knife, and more rarely still they are drawn out through the opening to protrude exteriorly as a fine vitreous filament. This condition may prove annoying and a source of danger. The temptation to pick up the filament with smooth forceps, draw it out further and cut it off should be resisted. The filament should be destroyed by actual cautery, by a chemical agent, such as trichloroacetic acid, or by electrocoagulation.

Movements of the Vitreous After Cataract Extraction.—The effect of vitreous surging in and out through the pupil after intracapsular extraction and the protrusion of vitreous into the anterior chamber are interesting. Conditions found after operation vary from a flat vitreous face posterior to the pupil to a mound or a mushroom-like protrusion through the round pupil or to a massive protrusion, particularly through the coloboma created by a complete iridectomy. If the vitreous is covered by aqueous and separated from the cornea and the limbus incision, to which it may adhere, it does no harm and may surge back and forth through the pupil with the movement of the eye without causing any damage. After a discission for after-cataract the same

features may be observed. The movements of the vitreous as described do not lead to detachment of the retina or to other complications.

Adhesions of the Vitreous After Cataract Extraction.—However, if vitreous has been lost and part of it has remained incarcerated in the wound, contractions may develop and opacities form. If the anterior chamber is slow in reforming and if the vitreous is actually in contact with the endothelial face of the cornea, particularly if the cornea has been injured by instrumentation, adhesion of the vitreous to the endothelium may occur, with hydrops of the cornea and subsequent intractable glaucoma. The condition is not amenable to treatment, and the only conclusion is that every effort should be made not to lose vitreous and not to injure the endothelium. Every effort should be made to have the anterior chamber reform as quickly as possible.

PLASTIC INFLAMMATION

Plastic inflammation of the iris and the ciliary body characterized by fibrinous exudates and small round cell infiltration of tissues may develop after operation from various causes, for example, chemical, mechanical or surgical trauma, sensitivity to retained lens cortex, development of low grade infection or allergic response of traumatized tissue to a distinct focus of infection.

Prevention of Inflammation After Cataract Extraction.—General examination of the patient before operation should include a search for foci of infection. Operation should be delayed in the face of a positive Wassermann reaction, active tuberculosis or nontuberculous granuloma, and also when the patient has a definite focus of infection in the mouth, throat, sinuses or bronchi or elsewhere. Many elderly persons exhibit foci which it may be wise to overlook if they seem to be carrying on well physically despite these foci. If they have arthritis, excessive fatigability, asthenia, fever, night sweats or other manifestations of reaction to infection, it will be necessary to delay the operation and clean up the foci as well as to build up the general condition. Blood counts and an estimation of the sedimentation rate may be of value in determining the prognosis for such patients. A lead to possible allergic response to surgical trauma may be obtained by intracutaneous tests with various bacterial proteins. Streptococcus filtrate, staphylococcus toxoid, typhoid vaccine, old tuberculin, brucellergen and other agents, in addition to lens protein, may be used for intracutaneous tests. If positive reactions occur, an indication of the degree of allergy may be obtained from the severity of the reaction. The reacting agent may then be used for desensitization by repeated, progressively stronger intracutaneous or subcutaneous doses. Typhoid vaccine may be used subcutaneously after an intracutaneous test; the method is similar to that used for immunization. Intravenous typhoid vaccine in small doses,

causing a severe reaction, is not well tolerated by elderly patients before operation. Typhoid H antigen may be used with greater safety.[17] In the face of iridocyclitis following operation, shock therapy may be accepted more gracefully, but preoperative shock therapy is not advisable. A nontraumatizing technic should be developed by the surgeon.

Focal Infection.—The indiscriminate removal of teeth or tonsils, the opening of sinuses, etc., shortly before operation for caatract is not indicated even though infection seems to be present. A stage of lowered resistance may set in, and the elderly patient may be less well prepared for operation than if a policy of nonintervention had been followed. If in certain cases it seems necessary to open or remove foci, this should be done sufficiently in advance of the cataract extraction so that the resistance may be recovered in time.

Use of Cycloplegics After Extracapsular Cataract Extraction.—As if in anticipation of iridocyclitis, it has been a time-honored custom to instill atropine sulfate solution after extracapsular extraction. There is hardly any question that in the experience of most surgeons the degree of plastic inflammation is greater after the average extracapsular than after the average intracapsular extraction. Atropine may be used in the average case at the subsequent dressings. Only occasionally does drug sensitivity, conjunctivitis or dermatitis develop. It may be well to use a coating of plain white petrolatum on the skin to protect it from drugs and secretions and to use a substitute cycloplegic for the atropine sulfate. Cocaine or epinephrine hydrochloride (1 : 5,000) may act as an adjuvant to facilitate the absorption of the atropine. Occasionally an epinephrine pack or epinephrine bitartrate may help in the dilation of the pupil and release of posterior synechiae when iridocyclitis is active.

Further Treatment in the Presence of Inflammation.—Hot compresses are valuable in allaying the sense of irritation and discomfort and in promoting healing. Acetylsalicylic acid and sodium salicylate are useful and may be administered to the limit of tolerance of the patient. Sulfanilamide and allied drugs have not been found to help much in the treatment of plastic inflammation of the eye. Dietary, hygienic and eliminative measures all help.

Postoperative opening of foci is to be done with great caution. Paracentesis of the anterior chamber after nonspecific protein therapy may prove of great benefit in changing the content of the anterior chamber, bringing in fresh antibodies from the blood serum. Knowledge of the sensitivity of the patient to the particular agents to be employed will help much in avoiding unpleasant and dangerous reactions.

17. Brown, A. L.: Use of Typhoid H Antigen Before Intraocular Operations, Arch. Ophth. **19**:181-183 (Feb.) 1938.

The eye of the average patient suffering from iridocyclitis after extraction (whether intracapsular or extracapsular) may recover sufficiently and the pupil clear well enough to permit excellent vision. However, after such an inflammatory reaction a secondary membrane or an after-cataract is to be expected, and discission is necessary to provide a clear pupil for satisfactory central vision.

Sympathetic Uveitis.—Sympathetic uveitis [18] may follow operation for cataract. The surgeon is aware of this possibility and cautiously avoids undue trauma to any portion of the uveal tract.

INFECTION

Under this subject will be considered the purulent inflammation of the eye which may follow operation for cataract.

Predisposition to Infection.—Patients with low vitality, low resistance or diabetes should generally be prepared long before they are subjected to operation. Any recent general infection, e. g., of the upper respiratory tract, should cause delay of any surgical procedure until complete recovery has occurred.

The clinical condition of the lids and appendages has much to do with the decision to operate and with the method of procedure. If the adnexa are clinically unclean the operation may well be deferred. Any acute inflammatory process of the eye necessarily contraindicates operation until the tissues are free from organisms. In the presence of chronic conjunctivitis, keratitis, blepharitis, dermatitis, dacryoadenitis or dacryocystitis, operation should be deferred. The patient should receive local and general treatment to clear up the process before operation.

Preoperative Treatment of Patients with Manifest Infection.—Local application of fresh 0.25 per cent silver nitrate, massage, curettement, ultraviolet irradiation, administration of vaccines and operation (including dacryocystectomy when indicated) are all measures which may be used. If chronic purulent dacryocystitis is present, dacryocystectomy rather than dacryocystorhinostomy is indicated.

The indiscriminate and routine use of strong antiseptic solutions in all cases, whether the field is clean or unclean, is not to be advocated. Silver nitrate, for example, if allowed to deteriorate and evaporate from the stock bottle may in an unknown strength cause considerable exfoliation of the conjunctival and corneal epithelium, devitalize the tissues and lead to lack of resistance to infection. The same may happen after lavage with large quantities of various solutions of mercury. The eye has a great natural resistance to infection, and if this is not

18. Joy, H. H.: Sympathetic Ophthalmitis Following Intraocular Operations, New York State J. Med. **36**:1498-1502 (Oct. 15) 1936.

diminished by chemical trauma the tissues will generally react well. This is fortunate, for all know that it is impossible to prepare a truly aseptic field for an ocular operation.

Prevention of Infection.—Clinical and laboratory research for the evaluation of factors leading to infection after intraocular operations is important. Records should be kept of the clinical condition of the eyes and adnexa. Smears and cultures may be made of material from the skin, lid margins and conjunctiva. Operation is not necessarily contraindicated for clinically clean eyes even when bacteria which are pathogenic as judged by laboratory criteria are found in the cultures. Bacteria may be present in the individual patient's tissues, or they may be brought to the patient by the surgeon or by others in the operating room. In the average operating room, even with the best precautions, there is a certain amount of dust and dirt which settles down when the room is not in use. The activity of the personnel moving in and out and about the room stirs it up again. The premises should therefore be washed with an antiseptic solution before the operation. The street clothing and the shoes of all personnel should be changed before they enter the operating room. Sterilization of the air of the room during the operation was attempted by Lister with antiseptic sprays, and work is now being done on the use of ultraviolet radiation for the same purpose. Effective local doses of ultraviolet radiation applied to the eye for the destruction of bacteria during operation would probably result in an abiotic reaction of the eye, particularly of the cornea, which absorbs ultraviolet radiation. The careful sterilization of instruments, the handling of instruments, the scrubbing of hands and arms and the use of caps, mask and sterile dressings are all important.

Sterilization of Instruments: Both sharp and nonsharp instruments may be sterilized by dry heat at 160 F. for thirty to sixty minutes without causing deterioration of the instrument or by boiling for five minutes. Gauze, cotton, gowns, towels, etc., require autoclaving at 15 pounds (6.8 Kg.) of pressure for thirty minutes.

Sharp instruments, such as knives and scissors, may be cleaned of all greasy preparations and immersed in 70 per cent grain alcohol solution for thirty minutes. Post [19] has shown that other solutions are more efficient and less injurious to the blades of instruments than alcohol. The solution advocated by Post is as follows:

Cresol U. S. P.	2 parts
Solution of formaldehyde U. S. P.	2 parts
Thymol U. S. P.	2 parts
95 per cent ethyl alcohol	94 parts

19. Post, M. H.: The Sterilization of Sharp Instruments by Chemical Solutions, Tr. Am. Ophth. Soc. **38**:37-53, 1940.

In practice this solution is placed in a small sterile dish on the operating table, and the knives and other sharp instruments are immersed in it for about fifteen or twenty miutes, though five minutes is sufficient in case an instrument is dropped on the floor and it is desirable to put it back into use shortly. Post stated that it is wise after removing the instruments from the solution to pass them through sterile water in order to avoid the possibility of any of the solution remaining on the instrument when it is used. As one can readily see, it would be serious if any of this solution were carried into the eye. This is especially true of jointed instruments, such as scissors. The solution apparently has no bad effect on the instruments, even after very lengthy exposure, and Post expressed the belief that it will prove equally highly germicidal and without particular irritating effect on the hands.

The nonsharp instruments may be boiled for three to five minutes. Lancaster [20] found that immersion by dipping in boiling water of single instruments for a brief period of fifteen to thirty seconds killed all pathogenic bacteria on microscopically clean surfaces.

The cleansing of the hands and forearms of the surgeon, assistants and nurses by scrubbing and cleaning for five minutes with a good brush and soap followed by immersion in 70 per cent grain alcohol solution and finally by drying with a sterile towel before putting on the sterile gown should be done as a minimum. Rubber gloves may be worn by all. At least, the nurse or assistant who makes up the moist cotton spindle wipes should use gloves in their preparation. Surgeons and assistants who do not wear gloves should never touch with their fingers the points of instruments which enter the eye. Instruments which have touched parts which may be unclean, for example, the skin or the lid margins, may be resterilized by holding them in boiling water, but unnecessary continued dipping of instruments by the surgeon and his first assistant detracts from their conduct of the operation. The surgeon should not take his eyes off the field of operation or permit the unwatched patient to do things which may endanger his eye in a brief fraction of time.

Caps should be worn to keep dust and dandruff from falling from the head. Masks, to be ideal, should be imperforate by test. Gauze or cloth masks even of considerable thickness may readily pass bacteria from the nose and mouth. Masks made of plastic and paper compounds may be fitted away from the face and, combined with a gauze mask over the nose and mouth, may prove to be the best. However, they may be bulky and cause clouding of the spectacles of the surgeon if these are worn, particularly if there is any excitement on his part. Experiments by the individual surgeon will determine which type of

20. Lancaster, W. B., in discussion on Post.[19]

mask is best for him. If it were not for the difficulty of instrumentation and the reduction of visibility, one might well adopt the method used for tissue culture and bactericulture, of operating under a special glass shield. Fortunately intraocular infections are rare after operation, and the general conduct of the operation and its many factors must take precedence over the single item of the prevention of infection, the latter being handled in the best manner possible by the individual surgeon. For the sake of his peace of mind and for the protection of the patient, his method should at least conform to the best practice in the community in which he operates.

General Chemotherapy.—There is no need for the routine use of sulfanilamide and allied drugs before or after operation. The fact that these drugs are known to stop bacterial growth in acute infections does not justify their use as a prophylactic for clean lesions. When indicated, the use of these valuable drugs should be checked by blood counts and by the estimation of blood level of the drug after it has been employed. If an infection appears to be starting, the responsible organism may be recognized by the clinical appearance and by the rapid examination of smears and culture. Sulfanilamide may be used for infection with Streptococcus haemolyticus. It has little action on Streptococcus viridans. Sulfapyridine or sulfathiazole may be used for pneumococcic infections, infections due to Bacillus pyocaneus and staphylococcic infections. Postoperative purulent infection of the eye directly indicates the use of these drugs, but before the bacteria can be conquered the ravages of the infection may have destroyed the functions and structures of the eye. Eyes have been salvaged by this means with greater or lesser function, however, when from the clinical condition complete loss seemed inevitable. The use of foreign protein shock therapy has little beneficial effect in the face of a severe infection, but in an emergency it may be used alone or in combination with chemotherapy. The surgeon must bear in mind the general condition of the patient and the possibility of an untoward or asthenic reaction from protein shock therapy.

Preparation of the Field of Operation.—Various routine procedures are in vogue for reduction of the incidence of infections, for example, clipping the eyelashes, at least those of the upper lid near the outer canthus, where they are not held out of the way by the guards of the speculum. Cleansing of the skin should include washing of the face with good soap and water before entrance to the operating room. The dry skin, brows and lid margins, including the lashes, may in the operating room be painted with half strength tincture of iodine. This may be followed by 70 per cent alcohol on gauze sponges. A spiral method of application should be used, starting from the skin of the eyelid and

working out to the periphery of the field which is exposed after the sterile towels and drapes are applied. An extra touch is the use of a suture pad of gauze or cotton cloth with an opening in it about the size of the operative field.

Aseptic Technic.—During the operation the surgeon should be very careful not to touch the skin or the conjunctiva with the points or blades of the instruments which enter the eye. After an instrument has been used it should be cleaned of blood by the instrument nurse and held in boiling water for thirty seconds before being used again.

Clinical Picture of Infection of the Eye Following Operation for Cataract.—The effects of contamination of the operatively treated eye may not be immediately evident. Some eyes destroy pathogenic organisms and do not permit them to develop. Other eyes modify the bacterial growth so that an insidious or a low grade plastic inflammation is produced, while in still others the same bacteria will multiply rapidly and with great virulence produce a fulminating infection. In the last-mentioned case the patient may well experience discomfort and pain and both eyes may lacrimate and discharge pus. The lids and the conjunctiva show more or less edema; the cornea, the anterior chamber and the iris become hazy, and there may be foci of pus near the sutures or on the iris, or the pus may sediment in the aqueous and collect in the lowermost portion of the anterior chamber in the form of hypopyon. Usually the infection is not limited to the anterior segment but quickly spreads to the posterior segment of the globe.

Procedures in the Event of Infection Following Operation.—The early removal of a suture which seems to be a focus of infection is indicated. The infection may rapidly progress from purulent endophthalmitis to panophthalmitis. Fortunately the development of sympathetic ophthalmia [21] has rarely been reported as a further complication of purulent infections. While one must realize that sympathetic uveitis may follow panophthalmitis, it is rarely necessary to rush to eviscerate the globe unless it is evident that the infection has produced a general reaction. If the surgeon recognizes that the eye is gone beyond recovery and wishes to spare the patient needless suffering and materially shorten the period of recovery he may eviscerate the globe. At an early stage in the infection the reopening of the limbus incision or the performance of a paracentesis may help in drainage and may abort the infection. However, there seems to be no possibility of exerting much influence on a severe infection by irrigation of the anterior chamber even with an antiseptic solution. When it is decided that the eye is completely lost

21. Samuels, B.: Panophthalmitis and Sympathetic Ophthalmia, Tr. Am. Ophth. Soc. **36**:69-77, 1938.

because of endophthalmitis or panophthalmitis the proper procedure is evisceration of the globe and not enucleation. In the latter operation the section of the optic nerve and its sheaths opens the way to possible meningitis and death of the patient.

SUMMARY AND CONCLUSIONS

The various general and local complications arising before, during and after operation for cataract and their prevention and handling are reviewed and discussed. The material used and the points raised are those which have been used in lectures on the subject. In general, the application is made in relation to my own custom and practice.

The important complications—hemorrhage, glaucoma, prolapse of the iris, incarceration of the iris, presentation of vitreous, loss of vitreous, inflammation, infection, imperfect healing of the incision and corneal opacity—are treated in detail. The only conclusion possible is that if a surgeon will by study, by observation of the experience of others and by analysis of his own experience broaden his knowledge of the prevention of these complications he will encounter fewer of them, and if he will increase his armamentarium for the handling of complications as they arise his results will be better.

Questions and Answers

TRAUMATIC PARALYSIS OF RIGHT SUPERIOR OBLIQUE MUSCLE

To the Editor:—A girl 16 years of age fell from a swing and was unconscious for two hours. Since that time she has had diplopia. A roentgenogram of the skull and orbit reveals fracture of the optic foramen through to the superior orbital fissure; no other neurologic abnormalities have been noted. The pupils are equal and react normally; the fields and the fundi are normal. The exophthalmometer reading for each eye is 14 mm. In the primary position the right eye is up 15 prism diopters; the deviation is greater on looking down and to the left. The right eye shows restricted depression. There is no deviation on looking up. With a red glass over the right eye the false image (red) is down and slightly to the right. The false image tilts to the left (intorsion). The patient's face is rotated down and to the left, and the head tilts to the left shoulder. The secondary deviation is greater than the primary, and the normal eye is down and to the right when the right eye is covered.

A diagnosis of paralysis of the right superior oblique muscle was made. There has been no change in the diplopia since its occurrence, five months ago.

What should be the general management of this patient? That is, how long should one wait before operating, and what would be the best surgical approach?

J. W. P., M.D., Michigan.

Answer.—It is most difficult to give an opinion concerning an extraocular muscle imbalance without personally examining the eyes. From the data given, however, it would appear that this is a case of traumatic paralysis of the right superior oblique muscle of five months' duration. In all probability the difficulty will not improve; still, the idea has long been prevalent that perhaps a year should be allowed to elapse before surgical intervention is undertaken in such a case.

As to treatment, exercise should be considered first. Rotation exercises in the field of the affected muscle performed daily for an extended period are often efficacious. If possible, it would seem best to omit padding of the affected eye, because this tends to discourage recovery. The same is true of the use of prisms. As a rule, prisms are not applicable in cases of frank paralysis of the extraocular muscles when the deviation is much greater in certain portions of the field of fixation than in others.

The prognosis for improvement by exercises or even by operation, of course, is dependent on how much power remains in the affected muscle. Surgical measures to be considered are: (1) tenectomy of the right inferior oblique muscle; (2) recession of the left inferior rectus muscle, and (3) advancement of the right superior oblique muscle as advocated by the late Dr. John M. Wheeler.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Biochemistry

DEXTROSE CONTENT OF CORNEA AND LENS UNDER EXPERIMENTAL CONDITIONS. R. WEEKERS, Compt. rend. Soc. de biol. **133:** 698, 1940.

Hyperglycemia produced by injection of dextrose increases promptly the dextrose content of the aqueous and after some delay also that of the cornea and the lens. Hypoglycemia produced by insulin reduces the dextrose content of the aqueous, the cornea and the lens. The concentration of dextrose in milligrams per hundred cubic centimeters of water content is as follows: for blood plasma, 159; for aqueous, 103; for the cornea, 120, and for the lens, 93. The dextrose content of the cornea is above that of the aqueous though less than that of the plasma, indicating the importance of the perilimbic capillary network in the nutrition of the cornea. The low dextrose content of the lens probably results from its metabolic consumption.

J. E. LEBENSOHN.

Conjunctiva

A CASE OF GAUCHER'S DISEASE WITH BIOPSY OF THE TYPICAL PINGUECULAE. T. EAST and L. H. SAVIN, Brit. J. Ophth. **24:** 611 (Dec.) 1940.

Together with the general symptoms of Gaucher's disease, on either side of the cornea of each eye were triangular pingueculae, rather granular in appearance and brownish yellow. The eyeballs were yellowish. A biopsy of the pingueculae was done. The microscopic study was made by H. A. Lucas, who gave the following description of his observations:

"Situated beneath the epithelium are small collections of large endothelial cells. The cytoplasm of these cells is degenerate, and shows a foamy appearance. The frozen sections show no fat-staining particles. The absence of fat-staining and the foamy appearance of the cells is similar to that observed in the endothelial cells of the spleen in cases of Gaucher's disease. The small amount of tissue available made further investigation impossible. The histological findings are compatible with Gaucher's disease.

"The case presents the features of Gaucher's disease, with involvement of the liver, and the usual slight anaemia, and typical pingueculae. The microspoic findings of the biopsy of the pingueculae are of interest, and we have not been able to find histological records of other cases. These lipoid deposits on the eyeball are so peculiar and striking that it seems worth while to draw attention to them."

The article is illustrated.

W ZENTMAYER.

Comparative Ophthalmology

THE FUNDUS AND FOVEA CENTRALIS OF THE ALBATROSS (DIOMEDEA CAUTA CAUTA-GOULD). K. O'DAY, Brit. J. Ophth. **24:** 201 (May) 1940.

O'Day describes the ophthalmoscopic appearances of the fundus of the eye of the albatross and of that of the giant petrel (Macromectes giganteus giganteus Gmelin). This is followed by a histologic study of the structure of the eye of the albatross. Especial interest attaches to the comparative differences between the deep central fovea of the bird and of the lizard and the shallow central fovea of man and of the primates. In those diurnal lizards in which the eye is not too small to allow such a maneuver, all three nuclear layers of the retina are pushed away from the center of the fovea so that no nuclear elements can come into the path of the rays of light reaching the center of the fovea. As a result of this, the cone fibers are elongated and there is a well marked layer of Henle. In addition, the outer segments of the foveal cones are greatly elongated and very slender and appear to lack oil droplets. The elongation of the cones results in the inward curving of the external membrana limitans, that is to say, with its convexity toward the vitreous. The more shallow fovea of man is constructed on the same principles—elongation and slimming of the visual cells to increase visual acuity without losing any sensitivity and the removal of structures which might impede the light rays falling on the fovea. The bird has attained its high standard of visual acuity while neglecting to a large extent these two apparently essential factors. Kolmer remarks that the retention of the oil droplets in the fovea and the presence of a possibly more accurate accommodative apparatus renders the lengthening of the "cones" unnecessary. He cites Rochon-Duvigneaud in support of his contention that the oil droplets would tend to correct any aberration. The incomplete baring of the foveal area of the bird would seem to support the theory of Walls that the function of the foveal depression is not to remove obstacles from the path of the light falling on it but to scatter it over a wider area.

The article is illustrated.

W. ZENTMAYER.

Congenital Anomalies

RARE OCULAR DEVELOPMENTAL ANOMALIES IN ASSOCIATION WITH CONGENITAL AND ACQUIRED BLINDNESS: CLINICAL "PROOF" OF VITREOUS DEVELOPMENT. J. H. YOUNG, Brit. J. Ophth. **24:** 597 (Dec.) 1940.

The patient was a man 21 years of age. He was totally blind. The right eye had become blind three years previously, after a severe attack of pain and inflammation. A tentative diagnosis of uveitis complicated by secondary glaucoma was made. The left eye was congenitally blind and exhibited the following conditions:

Primitive optic "disk" with absence of the nerve head, no lamina cribrosa and a narrow bore optic cup of great depth; complete absence of the normal retinal vascular system in the nondetached and detached portions of the retina and the optic cup and complete absence of neuronal development; partial achoroidia on the temporal side and a maldeveloped

choroid on the nasal side, in association with pigment deposition of an unusual type; rudimentary gray ciliary body (gray color due to the absence of pigment epithelium, normally developed from the neural ectoderm); partial aniridia; luxatio lentis (probable ectopia vera), associated with abnormal physical shape and structure with an auxiliary blood supply; a perfect vitreous; no evidence of any remains of the primitive hyaloid vascular system (this negative evidence is valuable, since retinal circulation is an outgrowth from this primitive system of vessels).

The author gives a diagnostic summary showing the stage at which the various lesions developed and also an embryologic interpretation of the findings. He states that the absence of a ciliary body and a normal retinal circulation indicate that these structures took no part in the development of a perfect vitreous.

He assumed that the lens played but a passing role in the development of vitreous and that the only structure left to form the "secondary" vitreous is in the nonvascular lining of the optic cup, which, in view of its immaturity, must be due to the functioning of its primitive cells, acting by virtue of their inherent determination and their special nature.

A point of interest is the optical and physical perfection of the vitreous, which has been maintained in its augmented state despite the almost complete absence of vascular structures within the eye. Two possibilities suggest themselves.

1. The remnants of the choroid were sufficient to maintain the volume and physical structures of the vitreous at their maximum efficiency (all other vascular structures being absent).

2. The vitreous when fully determined in development requires no maintenance whatever and while hermetically sealed within the globe and not subject to pathologic interference retains its efficiency unimpaired.

The author accepts the second of these possibilities.

The article is illustrated.

W. ZENTMAYER.

Cornea and Sclera

PHYSICAL QUALITIES OF THE CORNEA OF THE PIG. B. NAUSCH, Arch. f. Ophth. **141:** 214, 1939.

The changes in shape occurring in the surviving cornea of the pig under the influence of pressure exerted against the endothelial surface were studied by an ingenious method. The cornea was mounted watertightly over a 6.9 mm. hole in a hollow brass sphere. The inside of this sphere was filled with water and connected with the pressure-creating system. The brass sphere with the cornea was submerged in a metal chamber completely filled with saline solution. The cornea, giving under the pressure exerted against its posterior surface, protruded into the metal chamber and displaced some saline solution into a narrow tube attached to and communicating with the chamber. The movement of the saline solution in this tube recorded accurately the corneal deformity caused by pressure against its back surface. The results obtained with this method do not lend themselves to abstracting.

P. C. KRONFELD.

PATHOLOGY AND PATHOGENESIS OF RODENT ULCER OF THE CORNEA. Y. KOYANAGI, Arch. f. Ophth. **141:** 358, 1940.

An asthenic Japanese boy aged 15 at first presented the peculiar picture of circular episcleritic infiltration next to the limbus of each eye. Out of this picture marginal ulcers developed, which at first responded to local treatment but later became slowly progressive. The progression occurred primarily along the limbus and secondarily toward the center of the cornea. The central edge of the ulcer became undermined. After four months of observation in the ophthalmic clinic the patient had general malaise, low grade fever, blood-tinged sputum and a persistent cough. He was transferred to the medical clinic, where he died one month later. Autopsy revealed extensive bronchopneumonia and no signs of tuberculosis. At the time of death the corneal ulcers had a horseshoe shape, with a maximum width of 3 mm. The peripheral edges were clean and well vascularized, whereas the central edges appeared progressively affected. The outstanding histologic feature was active and very irregular proliferation of the corneal epithelium, which invaded the granulation tissue that lay at the floor of the ulcer (pictured). According to Koyanagi, this epithelial proliferation had the character of destructive infiltrating growth and not that of a reparative process. Careful study of the limbic region revealed that the epithelial proliferation preceded the loss of corneal tissue. The author states: "I am therefore assuming that the active factor in the pathogenesis of rodent ulcer of the cornea is a peculiar growth of the basal layer of the corneal epithelium."

P. C. KRONFELD.

Experimental Pathology

EXPERIMENTAL HERPETIC KERATITIS IN THE RABBIT: II. THE CAUSE OF THE DIMINISHED CORNEAL SENSITIVITY. K. A. REISER, Arch. f. Ophth. **141:** 339, 1940.

Corneas of rabbits which had been inoculated with herpes simplex or vaccinia virus and 1 human cornea with serpentic ulcer were studied in flat sections. In all instances the leukocytic infiltration was found to follow preexistent linear radial tissue spaces. The corneal nerves also used these radial spaces to reach their destination and were there, from the beginning of the disease on, directly exposed to mechanical and chemical damage. The slight diminution in corneal sensitivity which occurs in most forms of keratitis was probably caused by this topographic relation between the infiltration and the corneal nerves. In some respects the histologic picture of herpetic keratitis differed from that of vaccinia and serpentic keratitis. In the latter two diseases the leukocytes tended to form a ring around the focus of infection, whereas in herpetic keratitis the infiltration remained diffuse. In herpetic infection the limbic region showed accumulations of leukocytes, small areas of necrosis and dilated lymphatics. The last-named phenomenon was especially marked in the neighborhood of the nerve trunks from which the corneal nerves originated. The changes at the limbus probably caused the marked loss of corneal sensitivity associated with herpetic infections.

P. C. KRONFELD.

General

COSMETIC CORRECTION OF FACIAL ASYMMETRY WITH PRISMS. J. P COWEN, Am. J. Ophth. **23:** 60 (Jan.) 1940.

Cowen reports the case of a 14 year old girl whose left eye was amblyopic, esotropic and 8 mm. lower than the right. There was an extensive scar over the temporal region, the left upper lid and the upper lip, which resulted from irradiation of a hemangioma in infancy. Cosmetic improvement was effected by a 20 degree prism placed base down and in.

W. S. REESE.

General Pathology

A VASCULARIZED LAYER OF CONNECTIVE TISSUE SITUATED BETWEEN RETINA AND LAMINA VITREA. W. REICHLING and F. KLEMENS, Arch. f. Ophth. **141:** 500, 1940.

In a previous communication (*Arch f. Ophth.* **137:** 515, 1937) the authors described the occurrence in the otherwise normal eyes of persons over 50 years of age a thin layer of vascularized connective tissue which was situated between the retina and the lamina vitrea, behind the ora serrata. In this paper the authors report and demonstrate in numerous photomicrographs communications between the vessels of this connective tissue layer and the choroidal vessels. These communicating vessels pass through holes in the lamina vitrea.

P. C. KRONFELD.

Glaucoma

CYCLODIATHERMY PUNCTURE IN CASES OF GLAUCOMA. A. VOGT, Brit. J. Ophth. **24:** 290 (June) 1940.

"C. D. P." (diathermy puncture of the ciliary body) has now been employed by Vogt and his assistants for three years. The operation can seriously compete with the several operations employed for chronic primary glaucoma to secure subconjunctival filtration.

Neither sympathetic ophthalmitis, which is especially frequent after trephining and iris inclusion, nor panophthalmitis has been observed. Needles to be used to avoid injury to the cornea and lens are described. The first operation is performed from below. Procaine hydrochloride and epinephrine are employed subconjunctivally. A conjunctival incision extending from the internal to the external rectus muscles is made, laying bare the insertion of the inferior rectus muscle. The tendon is narrowed by short incision on both sides. A girdle about 2.5 mm. in width just above the insertion and between it and the limbus is punctured with the diathermy needle (length, 0.5 mm.; thickness, 0.16 to 0.18 mm.), with use of about 60 milliamperes, in such a manner that the needle (furnished with a stop) is pushed into the sclera vertically and at intervals of 0.5 to 0.25 mm. and is left there for from one-half to one second. About one hundred punctures are made within the girdle described. No puncture should be nearer than within 2 or 2.5 mm. of the limbus.

The articles should be consulted for more detailed description of the operation.

Illustrations are presented.

W. ZENTMAYER.

Hygiene, Sociology, Education and History

STANDARDS FOR OUT-PATIENT SERVICE IN OPHTHALMOLOGY. C. BERENS, Am. J. Ophth. **22:** 870 (Aug.) 1939.

Berens gives the following summary of his studies.

"Standards for out-patient service in ophthalmology including administration, plan and equipment, admission of patient, clinic procedures, selection, and tenure and duties of the medical staff and lay assistants have been prepared and presented in order to facilitate the development of new clinics or the reorganization of established departments."

W. S. REESE.

THE DEVELOPMENT OF OPHTHALMOLOGY IN BOMBAY. J. N. DUGGAN and V. K. CHITNIS, Brit. J. Ophth. **24:** 213 (May) 1940.

This interesting historical article does not lend itself to abstraction.

W. ZENTMAYER.

Lacrimal Apparatus

A CASE OF CHRONIC GRANULOMA OF THE LACRYMAL SAC. H. B. STALLARD, Brit. J. Ophth. **24:** 457 (Sept.) 1940.

Stallard reports a case of chronic granuloma of the right lacrimal sac due to retention of a silver style for thirty-three years. The condition had previously been diagnosed as a malignant neoplasm. The mass was 2.5 cm. long by 1.5 cm. wide. A roentgenogram showed the presence of a metal style in the right nasolacrimal duct and some thickening of the mucosa of the right maxillary antrum. The mass was removed and the roentgen diagnosis confirmed.

There was no evidence of malignancy.

One illustration accompanies the article.

W. ZENTMAYER.

A CASE OF ACUTE INFECTIOUS DACROADENITIS. G. WENGREJENOWSKY, Vestnik oftal. **16:** 381, 1940.

A case of a systemic disease with the involvement of both lacrimal glands and the auricular and the submaxillary glands is reported. A soldier aged 25 entered the military hospital with complaints of general malaise and swelling of the lids. There was marked edema of the lids and face, with sensitivity of the lacrimal glands on palpation. Later the auricular and the submaxillary glands became enlarged and the edema spread to the neck and the upper part of the chest. The temperature was elevated, and there was an increase of the leukocytes, but there were no other abnormalities. All signs and symptoms subsided gradually (in about six weeks) with no treatment.

O. SITCHEVSKÁ.

Lens

GALACTOSE CATARACT. A. TALIERCIO, Ann. di ottal. e clin. ocul. **68:** 58 (Jan.) 1940.

The author studied the calcium, hydrogen ion concentration and metabolism of the lens in rats with cataract produced by 50 to 70 per cent galactose in the diet. In all the young animals treated lens opacities

developed after seven to nine days and became complete after twenty to twenty-two days. A slight increase in calcium was observed in the lenses of the animals given galactose, but only after opacities had appeared and chiefly in the lenses with mature cataracts (0.12 to 0.22 mg. per hundred cubic centimeters as compared with the normal, 0.072 mg.). The p_H showed a slight shift toward the alkaline side, becoming 7.32 to 7.49 in the lenses with mature cataracts (normal, 7.24). The metabolism as tested with the Warburg apparatus showed no change in oxygen consumption until the mature stage, when a slight reduction was noted. Anaerobic glycolysis, on the other hand, while not modified in the early stages, showed a marked increase in the mature stage. This might be explained as due to the formation of acid groups capable of forming carbon dioxide from the bicarbonates. The excess of gas formed in this would not, in this case, represent a true increase in glycolytic activity.

S. R. GIFFORD.

ENTOPTIC ANALYSIS OF A CATARACT DUE TO GOUT. OSTMANN, Arch. f. Ophth. **141:** 156, 1939.

The author describes in great detail the entoptic phenomena which he observed in himself during the regression of a bilateral cataract attributed to gout. The objective findings are not given. The regression occurred slowly and was attributed to balneotherapy and to the drinking of water from hot alkaline springs.

P. C. KRONFELD.

TWO CASES OF BILATERAL SPONTANEOUS DISLOCATION OF THE LENS IN CONGENITAL SYPHILIS. B. SZINEGH, Klin. Monatsbl. f. Augenh. **103:** 230 (Aug.) 1939.

Two sisters, aged 10 and 6 years respectively, had bilateral luxation of the lens into the anterior chamber and secondary glaucoma. The symptoms of the second eye of each girl developed independently from those of the first eye, in each case after headache, pain in the eye and vomiting. Their elder brother, aged 12, had no ocular symptoms, and his Wassermann reaction was negative, whereas this reaction was strongly positive for the girls. Two abortions occurred between the birth of the boy and those of the girls. This history prompts the author to consider the ocular disturbances of the two girls as the result of congenital syphilis. (By an error in the original article the age of the "second child" is given as 10 years and that of the "third child" as 16 years, which evidently should be 6.)

K. L. STOLL.

Neurology

EXPERIMENTAL STUDIES ON HEADACHE: FURTHER ANALYSIS OF HISTAMINE HEADACHE AND ITS PAIN PATHWAYS. G. A. SCHUMACHER, B. S. RAY and H. G. WOLFF, Arch. Neurol. & Psychiat. **44:** 701 (Oct.) 1940.

The article is summarized by the authors as follows:

1. Of 15 subjects in whom afferent impulses from the superficial tissues of the scalp on one side were blocked by procaine, histamine headache in 4 and headache due to pneumoencephalographic examination in 11 were the same on the two sides of the head.

2. In 12 subjects obliteration of the circulation of the scalp by a blood pressure cuff modified the intensity of the histamine headache. That the reduction in pain was due to raising the pain threshold by introducing a second pain (the tight cuff) is offered as a likely hypothesis. Of 5 subjects, obliteration of the temporal artery by manual compression reduced the intensity of the histamine headache on that side in 2 but had no effect in 3. Complete subcutaneous infiltration with procaine hydrochloride of half the anterior part of the scalp (frontal, parietal and temporal areas on one side), including presumably all the vessels of the scalp in that area, did not prevent severe histamine headache in the frontotemporal region, bilaterally, which was of equal intensity on the two sides.

3. Injection of histamine directly into the temporal artery resulted in homolateral temporoparietal headache in 2 subjects.

4. Ligation of the temporal artery on one side in 4 subjects and of the middle meningeal artery on one side in 7 subjects did not influence the intensity of the headache experienced on the two sides after injection of histamine.

5. In 7 subjects who had partial section of the sensory root of the fifth cranial nerve on one side (resulting in unilateral analgesia of the lower part of the face in 6), histamine headache occurred bilaterally.

6. In 7 of 8 patients who had complete section of the sensory root of the fifth cranial nerve (resulting in unilateral hemianalgesia of the face and anterior half of the scalp), histamine headache was not induced on the denervated area, but did occur elsewhere in the head.

7. In a subject with complete hemianalgesia of the face and head (resulting from a head injury), strictly unilateral hemicrania on the normal side of the head was induced by histamine.

8. Histamine headache was absent in the back of the head on one side, but was present elsewhere in the head in 2 subjects with lesions of the cervical portion of the cord, causing unilateral occipital analgesia.

9. Section of the seventh and the ninth cranial nerve, respectively, in 2 subjects did not affect the bilateral equality of the headache induced by histamine.

10. Section of both sympathetic trunks in 2 subjects (cervical portion in 1 and thoracic portion in the other) had no effect on subsequently induced histamine headache.

The conclusions reached were as follows:

1. Histamine headache does not depend on the integrity of sensation from the superficial tissues.

2. The extracranial and dural arteries play a minor role in contributing to the pain of histamine headache.

3. Cerebral arteries, principally the large arteries at the base of the brain, including the internal carotid, the vertebral and the basilar artery and the proximal segments of their main branches, are chiefly responsible for the quality and intensity of histamine headache.

4. Although there may be other less important afferent pathways for the conduction of impulses interpreted as headache following injection of histamine, (*a*) the fifth cranial nerve on each side is the principal

afferent pathway for headache resulting from dilatation of the supratentorial cerebral arteries and felt in the frontotemporoparietal region of the head, and (*b*) the upper cervical nerves are the most important afferent pathways for headache resulting from dilatation of arteries of the posterior fossa and felt in the occipital region of the head.

R. IRVINE.

Ocular Muscles

FUNCTIONAL TRAINING, AS AN AID IN THE SURGICAL CORRECTION OF STRABISMUS. O. B. NUGENT, Am. J. Ophth. **23:** 68 (Jan.) 1940.

After a discussion of four groups of cases, Nugent arrives at the following conclusions:

"About 50 percent of all cases of strabismus can be corrected by refraction, occlusion, atropine, and orthoptic training.

"Early operation is not necessary in a large percentage of cases, if training can be used regularly.

"It is of great importance to have the cooperation of the parents and teachers.

"Most patients, especially in the younger groups, should have orthoptic training before operation.

"All with but few exceptions should have postoperative orthoptic training.

"Functional training has its effect upon the visual centers and the centers controlling the movement and behavior of the visual organs.

"Early consideration of squint is of paramount importance, as surgery may be reduced to a minimum by starting those cases as early in life as possible."

W. S. REESE.

The Pupil

PUPILLOGRAPHY: ITS SIGNIFICANCE IN CLINICAL NEUROLOGY. OTTO LOWENSTEIN, Arch. Neurol. & Psychiat. **44:** 227 (July) 1940.

The pupillographic procedure is a method of recording the pupillary movements of the two eyes simultaneously and under darkened conditions. Its importance is derived from two basic facts: 1. The pupillary pathways have within the nervous system enormous extensions, both sympathetic and parasympathetic, which are in connection with many upper and lower parts of the central nervous system. 2. Lesions in different parts of these pupillary paths produce characteristic modifications of the pupillary movements and reflexes, which are disclosed by pupillographic examination.

The normal types of the pupillary reflex to light are discussed. Four constitutional types exist; they correspond to four types of centrally conditioned equilibrium between the sympathetic and the parasympathetic nervous system: sympathicohypertonia, sympathicohypotonia, parasympathicohypertonia and parasympathicohypotonia.

Practically, the most significant contributions of pupillography so far lie in its making possible: (1) differentiation between organic and nonorganic lesions and (2) the early diagnosis and hence prophylaxis of syphilitic lesions in the central nervous system.

R. IRVINE.

Refraction and Accommodation

SOME CASES OF TRAUMATIC MYOPIA. O. G. MORGAN, Brit. J. Ophth. **24:** 403 (Aug.) 1940.

According to the author myopia may develop after direct trauma to the eye and, according to the intensity of the injury, four different types may be distinguished, namely:

"1. Those due to spasm of the ciliary muscle associated either with spasm of the sphincter pupillae, or with traumatic mydriasis. In these cases 1 to 4 diopters of myopia may appear which last a few days as a rule, and then disappear without treatment or under atropine.

"2. Those due to partial rupture of the fibers of the suspensory ligament of the lens associated with iridodonesis. This may be responsible for 5 to 6 diopters of myopia which is often permanent, and does not disappear under atropine.

"3. Those due to changes in the lens itself. This is often variable in amount, and may be associated with astigmatism.

"4. Those due to more serious damage to the anterior or posterior coats of the eye, causing presumably some axial lengthening.

"Cases illustrating several of the groups are detailed, and also a case of glaucoma with a varying degree of myopia. Under pilocarpine the myopia disappeared. Operation was followed by four hugh detachments of the choroid, between two of which the retina was detached. These all subsided. Neither increased tension nor the myopia returned."

W. ZENTMAYER.

Retina and Optic Nerve

THE PATHOLOGY AND PATHOGENESIS OF SYPHILITIC PRIMARY OPTIC ATROPHY. J. E. MOORE and A. C. WOODS, Am. J. Ophth. **23:** 1 (Jan.) 1940.

Moore and Woods give the following summary:

"This paper critically examines the recent literature on the pathology and pathogenesis of syphilitic primary optic atrophy. The scanty pathologic data available throw little light on the pathogenesis of the condition, although they seem conclusively to demonstrate that optic atrophy is not due to actual syphilitic inflammation of the optic nerves dependent on the presence therein of the causative organism.

"The newer theories as to the pathogenesis of optic atrophy are five: (1) It may be due to the virus of lymphogranuloma inguinale. This theory has so far nothing to support it. (2) It may be due to vascular constriction, functional or anatomic, within the optic nerves, with subsequent nutritional disturbances leading to atrophy; and it may be relieved or arrested by the use of vasodilator drugs. This theory seems ill-founded, and is now largely abandoned. (3) It may be due to a disturbance of the interrelationship between the factors of intraocular tension and retinal arterial systolic and diastolic blood pressure (the latter dependent on systemic hypotonia). This theory, advanced by Lauber and Sobanski, seems unsupported by the observed facts. (4) It may be due to adhesive optochiasmal arachnoiditis. While this theory

may explain the occasional case, it certainly does not suffice for many others in which arachnoiditis cannot be demonstrated at operation or necropsy. (5) It may be due to the combination of neurosyphilis and nutritional deficiency. This theory has some clinical and more experimental backing, but requires much further study before it can be accepted.

"In short, it seems probable that the pathogenesis of syphilitic primary optic atrophy, so often (perhaps almost always) associated with tabes dorsalis, is identical with that of tabes dorsalis itself. This, in turn, is as yet unknown, though recent studies, especially in the field of nutrition, offer hope of its elucidation."

An extensive bibliography is appended.

W. S. REESE.

RETINAL DETACHMENT OCCURRING IN PRIMARY COMPENSATED GLAUCOMA. H. S. GRADLE and D. SNYDACKER, Am. J. Ophth. **23:** 52 (Jan.) 1940.

Gradle and Snydacker state:

"1. Three cases of retinal detachment occurring in glaucoma in which the intraocular tension had been lowered by miotics are reported.

"2. Review of the literature reveals the rarity of this complication.

"3. The theories of retinal detachment are reviewed and an effort is made to correlate their importance in these cases."

W. S. REESE.

HISTOLOGIC PICTURE OF OCULAR TUBERCULOSIS, WITH SPECIAL REFERENCE TO THE RETINAL DISEASE. F. W. MEYER, Arch. f. Ophth. **141:** 408, 1940.

On 91 pages the author reports in detail and discusses the relevant observations in 33 cases of ocular tuberculosis in each of which one eye became available for pathologic study. Seventy-four illustrations, most of which are photomicrographs, depict the most important clinical and histologic features. The author's observations may be summed up as follows: The histologic picture of tuberculous iridocyclitis was not uniform. In some cases the typical granulation tissue and caseation were observed, whereas in others a nonspecific infiltration prevailed which hardly permitted an etiologic diagnosis on the basis of the histologic picture alone. In later stages of the iridocyclitis the nonspecific picture was more common than in the earlier stages. In most cases of severe uveitis the sclera and the retina were also involved. Retinal periphlebitis was present in the majority of cases of iridocyclitis. Usually the iridocyclitis preceded the periphlebitis, but the opposite sequence also occurred. There was no important difference between the periphlebitis occurring without uveitis and the periphlebitis secondary to uveitis except for that in the former the tendency toward hemorrhages was more marked. The ophthalmoscopic picture was the same in both forms of periphlebitis. The anatomic substratum of the white sheathing of the retinal veins was a perivascular infiltration which invaded the vessel wall. These infiltrations, as a rule, were nonspecific in appearance. They were accompanied with proliferation of the cells of the vessel wall, which often led to narrowing of the lumen or even to complete

obstruction. Hemorrhages occurred either because of this venous obstruction or through erosion of the vessel wall by the infiltration. Often it was difficult to distinguish between a periphlebitic lesion and a retinal tubercle. Probably such tubercles occasionally developed out of primarily periphlebitic lesions. On the other hand, retinal tubercles sometimes originated from choroidal tubercles. The author observed perivascular pigment rings, which suggested the existence of perivascular channels functioning like lymphatics. The pigment in these instances must have come from the anterior segment.

The formation of collateral vessels near obstructed veins was common. Whether the periphlebitis was caused by the local presence of bacilli or merely by toxins could not be decided.

By the injection of tubercle bacilli into a ciliary vein (the method first used by Wegner) a typical periphlebitis could be produced in rabbits, in addition to chronic uveitis.

Thus the occurrence of a tuberculous form of retinal periphlebitis was proved again. In none of the author's cases was there any evidence of endarteritis obliterans, which Marchesani considered to be the cause of retinal periphlebitis.

With regard to the pathogenesis of tuberculous periphlebitis, the author admits the possibility of hematogenic infection but on the basis of his own findings considers the lymphogenic mode with the primary ocular focus in the anterior uvea to be the most common one.

"Finally, the question arises whether in every case there are unquestionable histologic signs which permit the diagnosis of tuberculosis. The answer is that in a large number of cases the diagnosis of tuberculosis can be made on the basis of the histologic changes. There are, however, cases in which the histologic picture is not characteristic. In such cases it is necessary to consider the entire clinical course and then to ask oneself whether there are other causes which may produce the picture under question. By this process it will nearly always be possible to make a correct etiologic diagnosis."

P. C. KRONFELD.

PROPHYLACTIC OPERATION IN CASES OF THREATENING RETINAL DETACHMENT. A. JESS, Arch. f. Ophth. **141:** 538, 1940.

Vogt, in his book on retinal detachment (Stuttgart, F. Enke, 1936), advised against operative closure of retinal holes without detachment because it often happens that the edges of the holes form spontaneous adhesions with the choroid. Amsler, Gonin's pupil, definitely recommended surgical closure of the tears if on observation during one to two months they prove to have no tendency toward spontaneous healing.

Jess reports 8 successful preventive operations (surface plus perforating electrocoagulation) in cases of definite or suspected retinal tears without detachment. The prophylactic operation is easier and more likely to be successful than is the operation for an established detachment. Jess also stresses the value of thorough ophthalmoscopic study in cases in which retinal holes are likely to develop. Suspicious areas should be treated just like definite through and through tears.

P. C. KRONFELD.

Trachoma

STUDIES ON THE INFECTIVITY OF TRACHOMA. L. A. JULIANELLE and J. E. SMITH, Am. J. Ophth. **23:** 62 (Jan.) 1940.

This article concerns the immunologic aspects of the rickettsia concept of trachoma. The following conclusions are made:

"1. The majority of sera from patients with trachoma tested in this study contained no agglutinins for Proteus bacillus, OX_{19} and OX_2.

"2. Patients' sera which caused agglutination did so only within the range observed among normal individuals.

"3. Sera from monkeys infected experimentally or from rabbits serving for testicular passage of the infectious agent were devoid of agglutinins.

"4. Sera from animals at the end of repeated, intravenous injections of trachomatous tissues similarly did not react with Proteus bacillus.

"5. Antiproteus serum of high titer did not neutralize the infectious agent of trachoma.

"6. The results of this study do not confirm observation by other workers on the occurrence of the Weil-Felix reaction in trachoma."

W. S. REESE.

THE GIANT FOLLICLE OF MEYERHOF. E. CORNET, Ann. d'ocul. **177:** 131 (March) 1940.

This lesion, described by Meyerhof, is formed by the confluence of trachomatous follicles of the limbus. Pascheff called it a corneal follicle.

It is always single and forms a large or small growth occupying all or part of the superior limbus. Above this one finds a fine vascular network, which may be invisible to the naked eye. This may be formed of two or three parts. In this case at each narrow part a vessel passes which completes the encirclement of each portion. There is generally little reaction about it.

The treatment of the follicle needs to be fairly delicate. The author at first employed the curet, but this was found too radical and tended to increase the amount of pannus. Later the authors dissected the follicle with scissors around its whole border. This was found most satisfactory. A bibliography is presented.

S. H. MCKEE.

Tumors

MALIGNANT MELANOMA OF THE CHOROID. H. C. WILDER and G. R. CALLENDER, Am. J. Ophth. **22:** 851 (Aug.) 1939.

Wilder and Callender give the following summary.

"There are 1,238 malignant melanomas of the eye in the American Registry of Ophthalmic Pathology at the Army Medical Museum which, with few exceptions, have been classified according to their cell type and fiber content. It is hoped eventually to have a thousand such cases that have been observed for at least five years postoperatively.

"Forming the basis of this report are 253 patients with malignant melanomas that have arisen in the choroid or ciliary body, who have

been followed at least five years after enucleation or who have died from metastases under five years. The total death rate for this group is less than 50 per cent.

"The prognostic value of classification both by cell type and fiber content is indicated by the consistent results demonstrated in tables 1 and 2 as well as in all our former tabulations. In the classification by histologic type the epithelioid cell appears to be the most malignant, the spindle-cell subtype A relatively benign. As would be expected, the mixed group, which in almost all cases contains epithelioid cells, is second in malignancy to the purely epithelioid tumor.

"In the classification by fiber content, malignancy of the tumor appears to be inversely proportional to the degree of intercellular invasion by argyrophil fibers.

"To present an example of the importance and practical application of utilizing both methods of classification: A mixed-cell tumor does not often metastasize if it is heavily fibered, but a moderately fibered mixed-cell tumor is far more apt to metastasize than is a spindle B having approximately the same fiber content.

"The outstanding facts brought forth by this study are that no deaths have occurred from any spindle-cell subtype A or fiber group-3 tumor and that the patient in all cases in which no argyrophil fibers appear among the tumor cells has died.

"It is concluded that the two classifications, used in conjunction with each other, definitely narrow the field of error in the prognosis of uveal melanoma."

W. S. REESE.

OCULAR PAPILLOMA. R. E. WINDHAM, Am. J. Ophth. **22:** 966 (Sept.) 1939.

Windham reports 9 cases of ocular papilloma. He reviews the literature briefly and concludes that of the various methods of treatment the Shahan thermophore gives the best results.

W. S. REESE.

CONTRIBUTION TO THE BIOLOGY OF THE MALIGNANT MELANOMA OF THE CHOROID. W. GILBERT, Arch. f. Ophth. **141:** 547, 1940.

Because of the uncertainty with regard to the tissue elements from which so-called sarcoma of the choroid takes its origin, Gilbert recommends the noncommittal term malignant melanoma for this tumor (the term generally used in the United States). The division of the course of malignant melanoma into four stages (introduced by Knapp seventy years ago), namely, (1) the stage of silent intraocular growth, (2) the stage of intraocular inflammation or of glaucoma, (3) the stage of peribulbar growth and (4) the stage of metastases, should be abandoned for many obvious reasons. In many instances metastases occur during the first stage. Stage 3 may directly follow stage 1. Small peribulbar growths may easily be overlooked despite careful inspection of the wound immediately after the enucleation and despite careful pathologic examination of the enucleated eye. Metastases that have developed during stage 1 may remain dormant until the primary tumor is removed. "I, therefore, recommend a classification that is based upon the biologic reaction of the bearer of the eye containing the tumor. . . . By virtue of this

reaction the body may be able to keep under control and to destroy disseminated tumor cells. . . . If the body loses this faculty of control the disseminated tumor cells turn into rapidly growing metastases." Gilbert thus distinguishes between a premetastatic stage and a stage of established metastases. The stage of established metastases can, as a rule, be recognized by clinical and roentgen examination. The diagnosis of stage 1 can at this time only be made tentatively and by exclusion. One advantage of this new classification over the old is that it conveys a more nearly correct (not too favorable or too unfavorable) idea with regard to the prognosis.

P. C. KRONFELD.

Uvea

ESSENTIAL PROGRESSIVE ATROPHY OF THE IRIS. M. H. POST, Am. J. Ophth. **22:** 755 (July) 1939.

Post defines and discusses essential progressive atrophy of the iris and briefly reviews the literature. He reports a case and gives the following conclusions.

"This case is of interest because of the long period over which it has been observed, rather than for any particular additional information that it gives as to the etiology of this condition. The recorded data are insufficient to determine whether or not arteriosclerotic changes preceded the iridodialysis. It would appear that stretching of the iris tissues played little part in the etiology, as these were not seen to be under tension when first observed. The only evidence of any inflammatory process having existed at any time was the presence of a few pigmented spots on the anterior capsule of the lens, seen through the dialysis in the iris below. These might possibly be interpreted to indicate a very low-grade inflammation involving the pigment layer of the iris at this point."

W. S. REESE.

MULTIPLE RUPTURES OF CHOROID WITH RETENTION OF GOOD VISION. H. NEAME, Brit. J. Ophth. **24:** 399 (Aug.) 1940.

The patient was a "riveter's boy" aged 19 years who suffered a blow in the left eye from the handle of a broom. The eye was congested; the pupil was oval, with a small rupture of the iris sphincter. Cells were abundant in the anterior chamber. Vision was 6/60. Four more or less central choroidal tears were present on the temporal side of the disk. The fovea lay nearly midway between the second and the third. There were some hemorrhage into the vitreous and some commotio retinae. The field showed three scotomatous areas. One month after the injury vision was 6/12.

Illustrations are included.

W. ZENTMAYER.

Vision

VISUAL DEFICIENCY AT U. S. NAVAL ACADEMY. R. HAYDEN and O. R. GOSS, U. S. Nav. M. Bull. **38:** 252 (April) 1940.

Normal vision is a prime requisite for watch officers in the Navy. It should not be necessary to wear glasses, because, in addition to the danger of breakage or loss, glasses become fogged in bad weather. The

present regulations for admission of candidates to the Naval Academy, effective in 1940, are: "Each candidate on entrance to the Naval Academy must have 20/20 vision in each eye and must submit to refraction under a cycloplegic. Any degree of myopia, myopic astigmatism, or more than two diopters of hypermetropia shall cause rejection of the candidate." A reserve of approximately 1 D. of hypermetropia is desirable on admission if the candidate is to pass the visual requirements at graduation.

J. E. LEBENSOHN.

Visual Tracts and Fields

STUDIES OF THE VISUAL FIELDS IN CASES OF EXPERIMENTALLY PRODUCED NIGHT BLINDNESS. W. RAUH, Arch. f. Ophth. **141:** 544, 1940.

Ten normal men who had volunteered for the experiment were kept on a diet free of vitamin A for six months. Only toward the end of this period did the men complain of slight discomfort. At the height of the vitamin deficiency they showed, in addition to the night blindness, marked contraction of the visual field for yellow. This contraction and the night blindness promptly disappeared on injection of vitamin A or carotene.

P. C. KRONFELD.

Society Transactions

EDITED BY W. L. BENEDICT

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

FRANCIS HEED ADLER, M.D., *Chairman*

WARREN S. REESE, M.D., *Clerk*

Feb. 20, 1941

Removal of a Nonmagnetic Foreign Body: Presentation of a Case. DR. EDMUND B. SPAETH.

The case that is presented illustrates a method of localization and removal of a nonmagnetic foreign body from the eye. The exact position of the foreign body, composed of copper alloy, was determined by roentgenograms taken in the anteroposterior plane after silver rings had been sutured about the limbus and about the approximate site of the foreign body. After the necessary measurements had been made a hinged flap sclerotomy anterior to the equator was done at the plotted site, and the embedded foreign body was removed from the choroid. Removal by aid of the endoscope and the biplane fluoroscope was out of the question, because the foreign body was hidden by an area of exudative chorioretinitis. The postoperative recovery was uneventful. The central visual acuity was 6/6 with correction.

DISCUSSION

DR. WARREN S. REESE: Was it difficult to inject air beneath Tenon's capsule? Did the subsequent roentgen examination reveal definitely the location of the foreign body?

DR. EDMUND B. SPAETH: The injection of air into Tenon's capsule was difficult. The examination showed definitely that the foreign body was not external to the sclera.

Clinical Observations on the Treatment of Squint. DR. JACOB B. FELDMAN.

This paper will appear in full in an early issue of the ARCHIVES.

Retrobulbar Injection of Alcohol in Cases of Acute Glaucoma: Presentation of Cases. DR. C. E. G. SHANNON.

Five cases are reported of painful absolute glaucoma treated with retrobulbar injection of alcohol.

Grüter was the first to advocate this treatment. His method is to inject 2 cc. of a 2 per cent solution of procaine hydrochloride into the apex of the orbit, between the external and the inferior rectus muscle. Five minutes later 1 cc. of 80 per cent alcohol is injected.

Within fifteen minutes the eyeball is entirely anesthetic. All the muscles become paralyzed, and the eye is rendered immobile. Only slight discomfort follows the injections provided the procedure is carried out carefully.

Case 1.—J. S., a man aged 47, injured his right eye in 1919. The lens became hazy and dislocated, and it was subsequently removed by Hansell. Glaucoma developed a year later (1921), and there was complete loss of vision within a few years. The eye, however, did not become painful until 1939. Injections of alcohol were given on two occasions, seven days apart, and the pain was entirely relieved. There has been no return of the pain for two years.

Case 2.—L. S., a white woman aged 62, gave a history of iritis in the left eye followed by secondary glaucoma. Blindness resulted, and the eye became very painful. An injection of alcohol was given. Little distress followed the procedure, and the patient has been quite comfortable since.

Case 3.—A. P., a woman aged 51 years, consulted me during February 1936. Examination revealed chronic simple glaucoma in the right eye. The left eye was blind, the tension being 70 mm. of mercury (Schiötz). A Lagrange operation on the right eye was performed and proved successful. The left eye became painful two years later, and the treatment, consisting of an injection of alcohol, was carried out. This was followed by complete relief of pain. The patient has been comfortable since.

Case 4.—A. M., a woman aged 60, consulted me in May 1940. Examination revealed absolute glaucoma in the right eye, in which the tension was 80 mm. of mercury (Schiötz), and chronic simple glaucoma in the left eye. Ten months later the right eye became painful, and an injection of alcohol was given. The patient has had but slight discomfort since.

Case 5.—P. W., a man aged 57, was admitted to the Jefferson Eye Clinic on Jan. 26, 1941, complaining of extreme pain in the left eye. The tension in the eye was 50 mm. of mercury (Schiötz), and the vision equaled 6/200. The vision decreased to bare light perception and finally disappeared altogether. An injection of alcohol was given on January 29, after which the pain was relieved temporarily. A week later the pain returned, and a second injection was given. The patient has not had discomfort in this eye since.

Grüter in 1931 reported 56 cases in which patients with glaucoma were treated by injections of alcohol and followed for five years. There were 6 unsatisfactory results.

Jaench in 1925 reported 29 cases, in all of which the results were satisfactory.

Scheffels in 1927 reported 3 cases in which the results were satisfactory.

Salvati in 1927 reported 3 cases in which the results were satisfactory.

Alexiades in 1928 reported 15 cases in which the results were satisfactory.

Fejer in 1932 reported 5 cases, with an unsatisfactory result in 1. In this case an intraocular growth was discovered only after injection and removal of the eyeball had been carried out.

Malkin in 1934 reported 26 cases, in 4 of which the results were unsatisfactory.

The contraindications to this method of treatment are (1) useful vision (2) intraocular growth and (3) sympathetic ophthalmia.

With the results generally favorable and the technic comparatively simple, it would seem that this method is far preferable to enucleation in affording permanent relief from pain in a blind eye.

DISCUSSION

DR. SYDNEY OLSHO: Is the tactile sense ever interfered with by these injections?

DR. C. E. G. SHANNON: No loss of tactile sense has been reported so far, nor has it developed in any of my cases.

DR. WARREN S. REESE: I should like to ask Dr. Shannon whether there was improvement after treatment in the cases in which blebs or bullae of the cornea were present.

DR. C. E. G. SHANNON: The bleb in case 5 is an intercalary staphyloma, and I believe that its development was purely coincidental. It has shown little change during the last two weeks. There were no complications whatsoever in these cases. The only complaints were occasional neuralgic pains in the temporal regions; no pain occurred in the eyeballs.

DR. FRANCIS H. ADLER: Does Dr. Shannon think that there is any possible danger of getting some of the alcohol into a nonseptic thrombus?

DR. C. E. G. SHANNON: I presume that there is some danger of that. As far as I could determine from the records, no such accident has ever occurred.

Sulfathiazole in the Treatment of Gonorrheal Disease of the Eye.
DR. CARROLL R. MULLEN.

Gonorrheal disease of the eye has been successfully treated in 5 cases at the Philadelphia General Hospital with sulfathiazole administered both internally and externally. The results of treatment with this drug have not varied from those achieved with sulfanilamide. The technic of treatment and the dosage were essentially the same. One grain (0.06 Gm.) of sulfathiazole per pound of body weight, not to exceed 100 grains (6 Gm.), daily was administered orally. The dose was graduated according to the patient's needs. Instillations of a 0.2 per cent solution of sulfathiazole were administered to the involved eye every ten minutes for the first twenty-four hours. Iced compresses, a solution of atropine sulfate and a Bullar shield were resorted to when indicated.

It is necessary that nurses employed on eight hour shifts cooperate to the fullest extent in order that satisfactory results may be obtained from this type of treatment. During the second and third twenty-four hour periods the treatment was tapered off. There were no unfavorable blood pictures or toxic changes in any of these cases. The longest period of treatment in any case was three days, at the end of which time the first of three successive negative smears was obtained. The

smears in the average cases were negative after the first twenty-four to forty-eight hours. No corneal complications resulted, and all the patients were cured.

DISCUSSION

DR. ALFRED COWAN: Since this method of treatment has been developed, gonorrheal ophthalmia seems to have become one of the "least to be feared" conditions of the eye. It is remarkable to see how much improvement is obtained in the first twenty-four hours even with the most severe involvement. Any one who has had experience in the treatment of gonorrheal ophthalmia and who has not seen this method of treatment carried out would not readily believe that the patient had ever had gonorrheal ophthalmia. Gonorrheal ophthalmia treated in this way can now be considered an ordinary disease of the eye. It responds more quickly than does ordinary acute catarrhal conjunctivitis.

DR. L. F. APPLEMAN: I should like to ask whether sulfathiazole taken internally alone would bring about results as good as those obtained when the oral administration is accompanied with instillations. Since the drug seems to be specific in the destruction of gonococci, would not internal use alone be sufficient? I was asked this question during my recent lectures at the graduate school. My own experience was so limited that I could not give a very definite answer. I should appreciate an opinion from some one who has had more experience than I have had with this type of treatment.

DR. FRANCIS H. ADLER: I should like to report some observations that Drs. Souders and Scheie, of my department, have made. I am sorry that they are not here to make this report themselves. They have found that sulfapyridine and sulfanilamide when injected into the blood stream come through into the primary aqueous rapidly and in concentrations which are equivalent in a short period to that in the blood. Sulfathiazole, however, does not come through into the primary aqueous. It is found in the plasmoid aqueous after tapping of the anterior chamber, but not in the primary aqueous. If one is dealing with an intraocular infection, therefore, I should say that sulfapyridine and sulfanilamide should be used, but not sulfathiazole (unless it is used locally, as in the cases reported).

DR. CARROLL R. MULLEN: From personal observations I believe that one could abandon the oral administration of either sulfanilamide or sulfathiazole and get equally good results with frequent local cold irrigations. However, I do not feel justified in taking this chance, because of the satisfactory results which have been obtained by the combination of oral intake and instillation of these drugs.

In the early clinical trials of sulfanilamide at the Philadelphia General Hospital by Dr. T. A. O'Brien about three and one-half years ago the oral dosage of this drug was about the same as that which has recently been advocated for it and for sulfathiazole. However, the irrigations were given much less frequently, and only when the number of irrigations was increased did the remarkable results become evident. The immediate results following the oral administration of sulfanilamide alone were not particularly satisfactory in the treatment of gonorrhea of the eye. The best results were obtained when the drug was instilled at ten minute intervals for twenty-four hours.

In carrying out this treatment one must always keep in mind the fact that gonorrheal disease of the eye is a local condition, unless of course there is a perforation with resulting invasion into the anterior chamber. The literature contains many reports of the rapidity of appearance of this drug in both the aqueous and the vitreous after either instillation or ingestion. Based on the type of treatment pursued at the Philadelphia General Hospital, my personal opinion is that the oral administration of these drugs does not greatly influence the good results obtained in the treatment of gonorrheal disease of the eye. I continue to favor frequent irrigations during the first twenty-four hours, and I believe that iced or cold irrigations are more efficacious than those which are warm.

Instillation of a solution of sulfanilamide before operation is not a new procedure. For more than three years I have used it preoperatively as a routine measure in all of my cases. I cannot recall the occurrence of any postoperative infection as a result of its use. I agree with Dr. Cowan that physicians no longer need to be apprehensive about the outcome of treatment of this disease.

Again I should like to stress the importance of adequate nursing. I have seen the technic described carried out in other hospitals, but have not seen any results as good as those recorded at Blockley. The end results in other hospitals were quite satisfactory, but the period of treatment was greatly lengthened. I believe that this was due to the fact that only one nurse was assigned to a patient. There is too much detail in this assignment for one nurse to carry out. When one considers that irrigations must be given every ten minutes; that iced compresses must be applied, and that when the patients are children they must often be restrained, fed, bathed and given other attention, it is easy to understand that one nurse cannot adequately fulfil all the requirements.

At the Philadelphia General Hospital two nurses are assigned in relays under the direction of an experienced head nurse who is well acquainted with the prescribed technic. I wish to emphasize the importance of competent nursing. I wish also to repeat that the irrigations must not be given *about* every ten minutes, but definitely every ten minutes, and the exact time of each irrigation should be recorded.

DETROIT OPHTHALMOLOGICAL SOCIETY

PARKER HEATH, M.D., *President*

EDMOND L. COOPER, M.D., *Recorder*

Jan. 23, 1941

Angiospastic Retinitis in Diffuse Arteriolar Disease and in Chronic Glomerulonephritis. DR. HENRY P. WAGENER, Rochester, Minn.

In the cardiovascular-renal diseases, including chronic glomerulonephritis, it seems most probable in the light of present knowledge that the pathologic changes observed in the retina ophthalmoscopically are

indicative only of the response of the arteriolar system to the disease process and not of dysfunction, in the ordinarily accepted sense, of the kidneys or any other vital organ. In the main, two types of arteriolar response or reaction can be seen: functional, or actively spastic, and organic, or sclerotic.

The functional, or actively spastic, lesions, which are characterized by generalized or localized constrictions in the retinal arterioles, are observed most characteristically in the presence of the hypertensive toxemia of pregnancy and of acute vasospastic disease with hypertension. They represent probably the response of the arterioles to a vasopressor substance in the circulating blood. They can disappear without residuals presumably more or less coincident with the elimination or cessation of production of the vasopressor agent. In may instances, if the localized spastic constrictions persist organic or structural changes occur in the areas involved, probably in the form of intimal hyperplasia or arteriolar necrosis, but it is not known how long the constrictions must persist before structural changes ensue. Sometimes relaxation of the spasms without visible ophthalmoscopic residuals may occur after a surprising length of time.

The medial hypertrophy type of organic change in the arteriolar walls may be interpreted as the response of the arterioles to the elevated pressure itself. It is characterized ophthalmoscopically by changes in the color of the arterioles and by arteriovenous compression, both of which are due presumably to the thickening of the walls of the arterioles. They are indicative usually of an elevation of blood pressure of considerable duration but not necessarily of marked degree. The lumen of any particular arteriole is apt to be uniform in caliber in the presence of this type of sclerosis. The addition to these ophthalmoscopic appearances of definite localized constrictions in caliber usually indicates that an active vasopressor element is present (if the constrictions are actively spastic) or has been present previously (if the constrictions have become permanent or sclerotic).

If such complications as arterial and venous occlusions are excluded, edema, hemorrhage and exudation into the retina are seen in association with the actively spastic and not with the sclerotic lesions of the arterioles. It seems most probable that these evidences of "retinitis" appear when the constriction of the retinal arterioles in general is sufficiently disproportionate to the elevation of blood pressure to result in a drop of capillary pressure below the point at which normal nutrition, or oxygen supply, of the capillary walls of the retina can be maintained. In this sense the development of "retinitis" may be regarded as evidence of decompensation of the retinal circulation. This "retinal decompensation" is often associated with decompensation in other organs, but it may occur independently or in advance of decompensation elsewhere. Also, it may not occur in the presence of decompensation in other parts of the circulation.

If it can be assumed that in most cases the grade of chronic arteriolar change visible in the retina is fairly proportionate to that present in the systemic arterioles, especially in those of the kidneys, the prognostic importance of this phase of the retinal picture can be readily understood. Presumably the retina or the kidney with previously normal arterioles

can recover more or less completely from an acute vasospastic episode which would result in permanent decompensation if the arterioles had been seriously damaged before the episode. Clinically this seems to be true in cases of primary hypertensive disease. Many patients with acute angiospastic retinitis without chronic arteriolar sclerosis, especially in the presence of the toxemias of pregnancy or in association with unilateral atrophic kidneys, make excellent recoveries. In patients with acute angiospastic retinitis with chronic sclerosis of the retinal arterioles, however, the condition usually runs the course of typical progressive "malignant" hypertension.

This prognostic difference does not hold true, however, of chronic glomerulonephritis. In the presence of this disease, a form of retinitis occurs which cannot be distinguished essentially from that associated with malignant hypertension and which has the same course and the same prognostic significance. More frequently, however, the retinitis is of the acute angiospastic type without chronic arteriolar sclerosis. The retinitis itself has the same tendency to subside as it does in cases of primary hypertensive disease, but from the general prognostic standpoint development of this type of retinitis indicates usually the terminal phase of the disease, probably because in the presence of already damaged glomeruli the kidneys cannot survive the further deprivation of blood supply caused by the acute angiospastic episode.

DISCUSSION

DR. FRANK WEISER: The ocular fundus is often a great help to the internist in evaluating progress in cases of diffuse arteriolar disease and of chronic glomerulonephritis. In these conditions there must be an acute spastic episode in addition to organic changes to cause death. Without the acute spastic episode the condition will merely remain chronic.

Hypertension of groups 3 and 4 should not be considered improved by therapy until the results in treated patients are better than those in untreated persons. Hypertension of groups 1 and 2 is just as apt to improve without treatment as with it.

DR. GORDON MYERS: I should like to ask Dr. Wagener whether he feels that he can distinguish ophthalmoscopically between pyelonephritic hypertension and essential vascular hypertension.

DR. HAROLD F. FALLS, Ann Arbor, Mich.: May I ask Dr. Wagener whether he can distinguish between hypertension of group 1 and hypertension of group 2 without a more complete knowledge of the patient than the fundus picture? Is it necessary to know the blood pressure, the level of blood urea, the degree of renal function, etc.?

DR. A. S. CRAWFORD: Regarding prognosis, will Dr. Wagener say something concerning surgical treatment in the presence of hypertension of groups 2 and 3?

DR. HENRY P. WAGENER, Rochester, Minn.: In our experience at the Mayo Clinic surgical intervention has not materially influenced the end results of hypertension of group 4. The best results are obtained with group 1 and, as Dr. Weiser pointed out, patients with this type sometimes do well without specific treatment. Dr. Crawford's question was along this same line. The ultimate prognosis of hypertension of

groups 1 and 2 cannot be definitely evaluated without observation for a prolonged period. The prognosis with group 1 is good anyway, but with groups 2 and 3 it is probably better after operation, especially if the vascular change is largely angiospastic. If the vascular change is entirely organic the prognosis is not as good. In this connection I feel that the test to see whether anesthesia will relax the spasm probably does not give a sufficiently accurate result to determine whether operation should be done or not.

In answer to Dr. Myers' question, I would say that ophthalmoscopically I cannot differentiate between pyelonephritic hypertension and essential vascular hypertension. The organic changes in a retinal blood vessel are due probably to the hypertension itself. Usually patients with pyelonephritic or unilateral atrophic kidneys ultimately have chronic hypertension, and then the changes in the fundus cannot be distinguished from those of essential hypertension.

Dr. Falls asked about differentiating between groups 1 and 2 by means of the fundus picture alone. I do not think that this is possible. Responsibility for classification rests with the internist. The ophthalmologist can tell only the condition of the fundus as he sees it. However, I doubt that hypertension associated with angiospasm, past or present, should ever be placed in group 1.

PARKER HEATH, M.D., *President*

EDMOND L. COOPER, M.D., *Recorder*

Feb. 27, 1941

A Systematic Discussion of the Pathology of Tumor of the Lid. DR. ALSON BRALEY.

In the past several years I have collected all cases of tumor of the eyelid which have come to my attention for the purpose of determining how frequently the various types of growth occur. Over 325 tumors have been observed, and most of these were removed even when some other form of treatment might have been just as effective, since it was desirable to study as many as possible under the microscope.

The incidence, according to type, was as follows: papilloma, 34 per cent; nevus, 17 per cent; carcinoma, 15 per cent; sebaceous cyst, 13 per cent; fibroma, 5 per cent; sudoriferous cyst, 4 per cent; hemangioma, 4 per cent; xanthelasma, 1 per cent; sebaceous gland adenoma, 0.5 per cent; Boeck's sarcoid, 0.5 per cent, and lupus vulgaris, 0.5 per cent.

Clinical differentiation of these tumors is frequently difficult, and often one must depend on microscopic examination to establish the diagnosis.

The Roentgenologic and Dermatologic Aspects of Tumor of the Eyelid. DR. CLYDE K. HASLEY.

(Illustrations in color of the common and some of the uncommon lesions of the eyelid were shown.)

Fifteen per cent of all tumors of the lid are malignant.

Basal cell tumors should be treated according to their size. Irradiation is the treatment of choice for small lesions. For larger lesions roentgen therapy and operation are equally effective, but the cosmetic results are better with roentgen therapy. Removal of a biopsy specimen from a basal cell tumor has been condemned as causing metastases, but actually it is safe if properly done. A pigmented tumor is the only kind that is likely to be spread by this procedure.

Squamous cell tumors are classified according to malignancy into grades I, II, III and IV. A tumor of grade I responds well to irradiation. A tumor of grade III or IV should have the benefit of early operation, a radical procedure being indicated even for a limited lesion. This form of treatment prolongs the life of the patient. In spite of all treatment, tumors of grade IV are 100 per cent fatal.

Melanoma is radioresistant and should be treated by complete excision. Removal of a biopsy specimen is dangerous.

Many failures in radiation treatment of malignant tumors of the eyelid are due to underdosing. A single hypermassive dose or divided daily hypermassive doses will result in a greater number of clinical and permanent cures.

Postirradiation cataract may follow treatment with radium, but it never results from roentgen therapy. The beta rays of radium are less penetrating than the gamma rays; protection against them is easily obtained with a lead shield. Lead 1 cm. thick is required to obtain 50 per cent protection against gamma rays.

In any case of malignant tumor of the eyelid good surgical treatment is to be preferred to inadequate irradiation and vice versa. The best results are obtained by close cooperation between the roentgenologist and ophthalmologist.

DISCUSSION OF PAPERS BY DRS. BRALEY AND HASLEY

DR. FRANK HARTMAN: Dr. Braley listed three types of hemangioma of the eyelid. Plexiform hemangioma is frequently observed in a nonmalignant form, and I should like to inquire on what basis Dr. Braley feels that it is malignant.

DR. HOWARD DOUB: Dr. Hasley has given a clear exposition of radiation treatment of tumor in the region of the eye, and in the main I entirely agree with him. For a good many years I have used contact therapy, employing platinum radium needles in a hard rubber holder for epithelioma about the eye. This is effective when the growth has not infiltrated too deeply. Because the radium is in close proximity to the lesion, it gives an intense local reaction without too much depth dose to the underlying structures. I have on numerous occasions used roentgen therapy with the massive dose technic, and I feel that it is excellent for deep-seated lesions. I have never seen the development of a cataract secondary to my radium treatment of a lesion about the eye.

DR. A. D. BEAM: I should like to inquire of Dr. Hasley what treatment he recommends for xanthelasma.

DR. HAROLD F. FALLS, Ann Arbor, Mich.: In spite of the fact that operation for a benign melanoma is dangerous, especially if the tumor is cut into, there are some such tumors which should be removed. Will Dr. Braley state the indications for removal?

DR. A. ALSON BRALEY: Probably not all plexiform hemangiomas should be considered malignant. In many instances the tumor may be benign, but since this type tends to recur locally I prefer to consider it as locally malignant. It is not often malignant in the sense that it metastasizes.

Dr. Falls asked about benign melanoma. The indications for removal of such a tumor are (1) increase in size, (2) cosmetic deformity and (3) interference with vision.

DR. CLYDE K. HASLEY: Xanthoma does not respond to irradiation. Treatment should consist of cauterization of the lesion with trichloroacetic acid, the acid being neutralized after it is applied by a solution of sodium bicarbonate. If cauterization with trichloroacetic acid is not successful, electrocoagulation is the method of choice.

DR. RALPH H. PINO: I have found that complete surgical excision of xanthelasma is as effective as any other form of treatment, and the cosmetic results are excellent. In my hands recurrence takes place more frequently after electrocauterization than after excision.

Book Reviews

Manual of Clinical Chemistry. By Miriam Reiner, M. Sc. Price, $3.00. Pp. 296, with 18 illustrations. New York: Interscience Publisher, Inc., 1941.

In a minimum of space this book gives good information on the technic of the routine chemical methods. It ought to be most useful to the trained chemical technician. Most of the methods reported are carefully selected, though many laboratories probably will use different methods or modifications of the methods reported, and the description of some methods might be more complete.

In the Presbyterian Hospital the Folin method for the determination of uric acid in blood and urine (Folin, O.: Standardized Methods for the Determination of Uric Acid in Unlaked Blood and in Urine, *J. Biol. Chem.* **101:** 111, 1933) is considered superior to the older method reported by Reiner.

The normal dextrose content of cerebrospinal fluid is given as 20 to 35 mg. per hundred cubic centimeters against the recognized value of 60 to 80 mg. (Bodansky and Bodansky in "Biochemistry of Disease" [New York, The Macmillan Company, 1940] gave an average normal of 61 mg. per hundred cubic centimeters for dextrose).

The nephelometric protein determination in cerebrospinal fluid is used more widely than the tyrosine method for protein, as given in the book, since the former is faster (Denis, W., and Ayer, J. B.: A Method for the Quantitative Determination of Protein in Cerebrospinal Fluid, *Arch. Int. Med.* **26:** 436 [Oct.] 1920).

The ferric chloride method for melanin is recommended. In the laboratory with which I am associated this method has been abandoned in favor of the Blackberg method (Blackberg, S. N., and Wanger, J. O.: Melanuria, *J. A. M. A.* **100:** 334 [Feb. 4] 1933), although neither method will detect melanin in early melanosarcoma of the eye.

In general, however, the book will undoubtedly be found useful in the clinical laboratories.

KARL MEYER, M.D.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Consolacao, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.
All correspondence should be addressed to the President.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Albert C. Snell, 53 S. Fitzhugh St., Rochester, N. Y.
Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank R. Spencer, Physician's Bldg., Boulder, Colo.
President-Elect: Dr. Ralph I. Lloyd, 14–8th Ave., Brooklyn.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. F. P. Calhoun, 478 Peachtree St. N. E., Atlanta, Ga.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Place: Hot Springs, Va. Time: May 29-31, 1941.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. John Evans, 23 Schermerhorn St., Brooklyn.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Vaillancourt, 46 St. Louis St., Quebec.
Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. V. May, 1703 Main St., Marinette.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield
Place: Wisconsin Rapids. Time: June 1941.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Isaac H. Jones, 635 S. Westlake Ave., Los Angeles, Calif.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Spencer S. Howe, 103 E. Holly St., Bellingham, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 419 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. E. Rideout, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. Franklin P. Maury, Professional Bldg., Tucson, Ariz.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. J. K. Heckert, 103 N. Washington St., Lansing.
Secretary-Treasurer: Dr. W. D. Irwin, 710 Hanselman Bldg., Kalamazoo.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. W. E. McClellan, 750 Main St., Hartford.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.
Place: Macon. Time: May 13-17, 1941.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S.E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGearv, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. A. L. Hammerel, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.
Place: Atlantic City. Time: June 3-5, 1941.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. N. A. Yourgs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Roderick Macdonald, Rock Hill.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.
Place: Columbia Hotel, Columbia. Time: November 1941.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. E. L. Goar, 1300 Walker Ave., Houston.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.
Place: San Antonio. Time: December 1941.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 628 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. George G. Hawkins, Newport News.
Secretary-Treasurer: Dr. Guy Fisher, 3 E. Beverley St., Staunton.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. James G. Fowler, 412 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Sanford Gifford, 720 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmologic Club

Chairman: Dr. Albert D. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Wallace W. Ralston, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. John I. Garret, 57 Stokes Bldg., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Paul Southgate, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Kirt G. Parks, 605 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Harold Mulligan, 1680 N. Vine St., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. Leonard C. Whiting, 121 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Algernon Reese, 73 E. 71st St., New York.
Secretary: Dr. Brittain Payne, 896 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. Morris Davidson, 80 Centre St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Harold Gifford, 1620 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Secretary: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. Edward A. Weisser, 119–5th Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave. Time: 5 p. m., Jan. 22. 1941.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. J. F. Hardesty, Missouri Theatre Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMOLO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Fred Boyle, 490 Post St., San Francisco.
Secretary: Dr. Frank Hand, 450 Sutter St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. R. Webster, State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. John R. Myers, State Tower Bldg., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. S. H. Patterson, 1251–15th St., Toledo, Ohio.
Secretary: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. Frank Costenbader, 1726 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. L. Conner Moss, 1710 Rhode Island Ave. N.W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.